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TORSION OF THE APPENDIX TESTIS* (HYDATID OF MORGAGNI)

Report of Two Cases

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TORSION of the appendix testis is so rare that the condition is seldom thought of in the differential diagnosis of lesions of the scrotum. No description of the condition can be found in textbooks on Urology with the exception of Hinman's recently published book[1]. The signs and symptoms are very similar to those seen in other acute diseases of the scrotum.

The first case report of torsion of the appendix testis was recorded by Colt[2] who, in 1922, described a case seen in the Royal Infirmary at Aberdeen, Scotland in August 1921. Albert Mouchet[3], a Frenchman, is credited with the first detailed pathological description of this condition and in 1928 he reported three personal cases. Dix[4], in a review of the literature in 1931, collected forty-seven cases. To date only two cases have been recorded in the North American literature, both from the Boston Children's Hospital by Foshee[5] in 1932. Since September 1934 two cases have been seen at the Massachusetts General Hospital.

The appendix testis is a remnant of the cephalic end of the Mullerian duct. It is a pea-sized structure, usually sessile but occasionally pedunculated, located near the upper pole of the testicle and is present in the majority of individuals. Normally, it is cystic, containing transparent liquid, and is lined with cylindrical epithelium[6].

REPORT OF CASES

CASE 1. C. Z., a thirty-nine year old Greek poultry-raiser, came to the hospital September 17, 1934 with the story that four weeks before entry he had been "kicked in the scrotum by a pet rooster". He immediately had severe pain in the left side of the scrotum accompanied by dizziness and nausea and found it necessary to lie on the ground for a few minutes. Throbbing pain in the left testicle kept him awake that night but was less severe on the following day. At this time the patient noticed swelling of the left part of the scrotum. His doctor advised rest in bed and ice packs to the scrotum. The pain gradually subsided but the swelling persisted and the patient was referred to the hospital. There were no urinary symptoms.

On examination the left side of the scrotum was enlarged four to five times its normal size. It was tense, smooth and did not transmit light. The testicle and epididymis could not be distinguished. There was very slight tenderness. The urine was negative and the temperature was normal.

Hematocele was thought to be the most likely diagnosis. Operation was done under spinal anesthesia. The scrotum was incised and the tunica vaginalis was freed and delivered. When opened, three to four ounces of dark blood and blood clot escaped. A round mass, the size of an English walnut and thought to be a necrotic testicle, was exposed. An orchidectomy was done by amputating the cord at the external inguinal ring. The scrotum was closed except for a small rubber drain.

Further examination revealed that the structure taken to be testicle was really the appendix testis. The tunica albuginea was thickened and covered with fibrin but the testicle and epididymis were normal.

CASE 2. I. G., a Jewish boy of eleven years, entered the hospital April 6, 1935 complaining of severe pain in the left lower quadrant and left side of the scrotum of forty-eight hours' duration. There was no history of trauma. There had been no nausea or vomiting and no change in bowel habits. The temperature was 100° and the white blood count 11,200.

On examination the left side of the scrotum was found to be enlarged twice its normal size and the overlying skin was reddened. The cord was not thickened. The child would not tolerate examination of the testicle because of tenderness.

A diagnosis of torsion of the testicle was made and operation was performed immediately under ether anesthesia. The tunica vaginalis was exposed and opened. About one ounce of clear, yellowish fluid was expelled. The testicle and epididymis were grossly normal. Near the upper pole of the testicle there was found a pedunculated, bluish, oblong mass about the size of an almond. (Fig. 1.) The twisted pedicle was clamped, ligated and divided and the mass removed. The scrotum was closed without drainage. Convalescence was uneventful and the child was discharged after five days.

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ETIOLOGY

The etiology of torsion of the appendix testis is obscure. The lesion occurs in individuals in whom this structure is pedunculated. Foshee[5] has suggested that a sudden and violent cre-

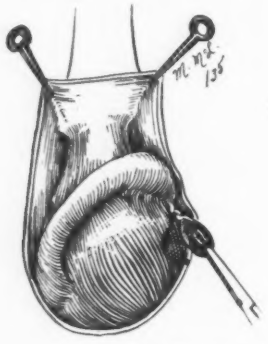

FIG. 1. The gangrenous appendix testis is held in the forceps.

masteric reflex is the probable cause of torsion of the pedicle. The history of trauma may be lacking.

INCIDENCE

The age incidence in sixty-one cases, of which fifty-nine have been collected from the literature, has varied between eleven months and sixty-six years. Only three cases have been more than sixteen years of age.

PATHOLOGY

Torsion of the pedicle results in necrosis due to the loss of blood supply. Foshee has described edema of the testicle and epididymis. In the two cases observed by the author there was no gross evidence of any change in the testicle or epididymis and in Case 1 these structures were microscopically normal. There is usually an accumulation of clear fluid within the tunica vaginalis. This fluid may be bloody as in Case 1. Culture of the fluid removed in Case 2 gave no growth. Necrosis was too advanced to permit histological study of the specimens from either of our cases. The gangrenous appendix testis may become detached from the testicle and be found floating free within the tunica vaginalis[7, 8].

SIGNS AND SYMPTOMS

The common symptoms are the sudden onset of pain in the scrotum which may radiate into the groin. The pain may be accompanied by dizziness and nausea and is usually followed by swelling and retraction of the scrotum on the affected side. The overlying skin may become reddened. There is often slight rise in the temperature and white blood count during the early acute stage. The symptoms are not always severe. Mouchet has described a case in which retraction of the affected side of the scrotum and syncope were the only signs.

DIAGNOSIS

The diagnosis of torsion of the appendix testis is difficult and seldom made before operation. This condition may be confused with acute epididymitis, orchitis or torsion of the testicle. Careful palpation, when tolerated by the patient, may reveal a small, tender nodule located near the upper pole of the testicle and distinct from the epididymis and testicle. The signs of inflammation and the elevation of temperature are usually more marked in acute epididymitis and orchitis. Both orchitis and acute epididymitis commonly occur in the presence of infection elsewhere, either in the urinary tract or in other parts of the body. Torsion of the testicle is likely to result in greater thickening of the spermatic cord.

TREATMENT

Granting that a diagnosis can be made without operation, the acute symptoms may be expected to subside gradually under palliative treatment. Early operation will confirm the diagnosis and hasten convalescence. The incision may be made in the inguinal region or over the scrotum as the operator chooses. In addition to the removal of the gangrenous appendix testis, excision of the redundant tunica vaginalis is desirable in the presence of a large amount of hydrocele fluid.

CONCLUSIONS

1. Two additional cases of torsion of the appendix testis are described.
2. The diagnosis is difficult and should be considered in all acute lesions of the scrotum, especially through the age of adolescence.
3. Operative removal of the strangulated appendix testis is the treatment of choice.

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EXPERIMENTAL AND CLINICAL OBSERVATIONS ON URINARY CALCULI*

BY C. C. HIGGINS, M.D.†

NUMEROUS clinical observations have been made which support the contention that a relationship exists between the formation of urinary calculi and a deficiency in the diet. The clinical observations of McCarrison[1] of India indicate that stone areas occur in parts of that country where a properly balanced diet is not followed. Similar observations have been made by Fujimaki[2] and other observers. In the United States, stone areas are said to exist in southern Florida and southern California, and in England, Joly[3] states that calculous disease is more prevalent in Westmoreland and Derbyshire. Joly also has stated that in countries where progress in the knowledge of diet and nutrition has occurred, we have been rewarded by a decrease in calculous disease in children, while in countries where the children do not have a well-balanced diet, calculous disease still is quite prevalent. Osborne and Mendel[4], in the course of a series of investigations dealing with dietary problems, noted that calculi developed in a certain percentage of the experimental animals. This was true, however, only of the rats that have been on a diet deficient in vitamin A during some part of the experiment.

I should like to review briefly the experimental work that we have been doing for the past four years.

The effect of the withdrawal or of a deficiency in the various vitamins was studied to determine the exact relationship between the production of calculi and a deficiency in the specific vitamins. Likewise, the effect of inadequate amounts of fat, protein, carbohydrate and the various salts was studied. In experimental work with dietary problems, extreme care must be taken in the preparation of the foods or a misinterpretation in results will occur. It is essential that the necessary proteins, fats and carbohydrates and the various salts be included in the diet and the food must contain the required number of calories and it must also be palatable.

After the rats have been maintained on a diet deficient in vitamin A for twenty-nine days, the first signs of vitamin A deficiency which are manifested are xerophthalmia, loss of weight and if small amounts of vitamin A are not restored to the diet at this time, the rats become cannibalistic, the stronger rats prey on the weaker and some die from intercurrent infection.

The incidence of urinary calculi that can be formed in the white rat that is maintained on a diet deficient in vitamin A is shown in the following table:

EXPERIMENTAL PRODUCTION OF URINARY CALCULI

200 ALBINO RATS—25 CONTROLS

Number of Rats	Duration of Experiment Days	Bladder Calculi	Per Cent
30	1-30	1	3
28	30-60	4	14
42	60-90	16	38
28	90-130	20	71
30	130-180	26	86
17	180-250	15	88

Twenty-five controls: 1 showed sand in bladder.

EXPERIMENTAL PRODUCTION OF URINARY CALCULI

Number of Rats	Duration of Experiment Days	Kidney Calculi	Per Cent
30	1-30	0	0
28	30-60	0	0
42	60-90	6	14
28	90-130	8	28
30	130-180	9	30
17	180-250	7	41

Twenty-five controls: No renal calculi.

EXPERIMENTAL PRODUCTION OF BILIARY CALCULI

Number of Rats	Duration of Experiment Days	Biliary Calculi	Per Cent
30	1-30	0	0
28	30-60	0	0
42	60-90	0	0
28	90-130	2	7
30	130-180	4	13
17	180-250	4	14

Twenty-five control rats: No biliary calculi.

It will be noted that bladder calculi form at an earlier period than do kidney calculi. Likewise, at the end of 250 days, small stones are found in the livers of these animals in from twelve to fourteen per cent of the cases.

The question also arises as to the possible relationship between infection and the formation of urinary calculi. In our experimental work it was found that the incidence of infection was practically equal to that of the calculus formation. The chemical analysis of stones showed that they were composed of calcium and magnesium phosphate with traces of carbonate. Neither uric acid nor oxalates were found to be present. There was also a small amount of mucoid substance.

When it had been demonstrated that stones could be produced by a diet deficient in vitamin

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A and that they could be prevented by the addition of vitamin A to the deficiency diet, the question arose regarding whether stones could be caused to undergo solution when vitamin A was restored to the diet. A group of rats, therefore, was maintained on a deficiency diet for a sufficient period of time to allow the stones to be demonstrated roentgenographically. These rats were then maintained on the same diet but cod liver oil was given daily by mouth by means of a medicine dropper. In every instance, if the rat survived for a sufficient period of time, the stones underwent complete solution and when autopsy was performed, no evidence of a calculus remained. The time required to cause a dissolution of the stone, however, seemed to depend directly upon the degree of infection present in the kidney and likewise upon the amount of kidney damage present which reduced the function of the individual kidney. In the absence of infection or any degree of renal damage, the stones underwent solution with considerable rapidity.

At this time, we decided to determine whether an alteration of the constituents of the diet would cause a change in the chemistry of the calculi which were produced. As I reported in previous communications[5, 6], when the phosphorus was reduced to a minimum, in comparison with the calcium present in the diet, the chemistry of the stones which were produced was changed considerably. The stones produced after the phosphorus intake was reduced were composed chiefly of calcium carbonate with traces of calcium magnesium phosphates. Again no uric acid or oxalates were present. We then decided to attempt to produce calculi in other animals whose diet had been deficient in vitamin A and a group of dogs was therefore studied. I was fortunate in seeing with a veterinarian a dog which had had stones in the bladder at frequent intervals and had had two previous cystotomies with the removal of stones from the bladder. Upon analyzing the diet of this dog, it was found that his diet was definitely deficient in vitamin A. Stones removed from the bladder were composed chiefly of calcium and magnesium phosphate with only traces of carbonate. In our experimental work with other dogs, after they had been maintained on a deficiency diet for a period of seven and one-half months, a cystotomy was performed. In four of the seven dogs that have been operated upon up to the present time, multiple stones were found in the bladder in three instances. One stone was allowed to remain in the bladder which was then closed in the usual manner as was the abdominal wall. These dogs are now on a diet high in vitamin A in an attempt to determine whether the stones produced in the dogs also will undergo solution.

At the present time, the work of the production of uric acid stones is being studied. This work is carried out on chickens and pure bred Dalmatian dogs, and a report of this will be published in a later communication.

From this experimental work, it seemed that we had sufficient data to permit us to apply our results in clinical cases. After considerable deliberation, we decided that the cases in the following groups might be suitable for medical treatment.

1. Cases in which the patient refused removal of the calculus by surgery.
2. Cases in which bilateral renal calculi were present but in which surgical intervention was not deemed advisable.
3. Cases in which calculi were present in one of the calices of the kidney but were not producing obstruction.
4. Cases in which small calculi were present in the renal pelvis but did not produce obstruction.
5. Cases in which calculi were passed at frequent intervals but could not be demonstrated roentgenographically.
6. Cases in which calculi were of sufficient size to require nephrectomy.
7. In orthopedic cases such as osteomyelitis or fractures where the recumbent position was required for a long period of time. It is known definitely that calculi may form under such conditions.
8. Cases in which prevention of the recurrence of lithiasis following operative removal of stones was desired.

The following routine has been adopted in cases where medical treatment is anticipated. The patients are hospitalized for a period of from three to seven days while the necessary examinations of the blood and urine and x-ray studies are made.

A plain roentgenogram and stereoscopic study is first made. These show whether stones are actually present, whether they are unilateral or bilateral, and whether coexisting stones are present in the ureter or the bladder. This is followed by a cystoscopic examination. After visualization of the bladder, catheters are passed to both kidney pelves. Specimens are taken in glucose brain broth for culture. Likewise, a specimen is collected in order that we may have a stained slide of the sediment. Two cubic centimeters more are collected for pH determination and the usual cytological examination. A fractional phenolsulphonephthalein function test is made.

In all cases, a catheterized specimen of urine is taken from each kidney for a pH determination. This is done in view of the fact that we have found in some instances (17 cases) a definite difference in the pH of the urine from a kidney containing a stone, especially if the stone is of the calcium-phosphate type. In

one instance, the pH of the urine from the kidney in which a stone was located was 8.4 and triple phosphate crystals were present, while in the normal kidney, the pH was 5.2 and no phosphate crystals were present. Therefore, it can readily be seen that the pH of the bladder urine is not always a true interpretation of the acidity or alkalinity of the urine as it comes from the kidney.

The following day after the spasm of the ureters which results from the passage of the catheters has subsided, an intravenous urogram is done. This shows whether stones are producing an obstruction and also gives additional information regarding the function of the kidney. If it is obvious that a definite obstruction is present or that the patient is having sufficient discomfort and pain from the presence of a stone, surgical intervention is necessary. It certainly would be unwise to temporize with an obstructive lesion of the upper urinary tract and to sacrifice the renal parenchyma while the patient is on the dietary régime.

Certain blood examinations are quite important. Calcium, phosphorus, phosphatase, urea, uric acid, creatinin and sugar determinations are made routinely. If an elevation of the blood calcium is found and a lowered blood phosphorus, our attention is drawn to the possibility of the presence of parathyroid disease and the patient is studied more closely along this line. Likewise, if there is an elevation of the blood uric acid, naturally it is important that the purines and the various foods in the diet that tend to elevate the blood uric acid be minimized. If the patient has passed a calculus previously, this is analyzed in our chemical laboratories. A routine Jeans test is made in order to determine whether clinical evidence of vitamin A deficiency is present.

After all these data have been secured, we can tell whether the patient is suitable for conservative treatment and the high vitamin A acid-ash diet is prescribed. Vitamin A is given in the form of two Carotene-in-oil capsules three times a day for a period of one month. After this time, one capsule is taken each morning and night.

Patients must follow the diet for a considerable period of time. Because it is so essential that the patient should understand the principles of the diet, the dietitian visits him daily while he is in the hospital to discuss with him why certain foods are allowed and others restricted. She also explains in detail the sample menus which the patient is given to follow when he leaves the hospital. It is impressed upon the patient that if satisfactory results are to be secured, the diet must be followed as closely as a diabetic patient adheres to his diabetic régime.

No specific diet can be used in all cases but the diet must be prescribed in each individual case depending upon the pH determinations of the urine and the blood chemistry. As a general rule, we start with an excess of acid- or alkaline-ash of approximately 17.3 cc. depending upon the pH of the urine from the kidney harboring the calculus. However, in the presence of a proteus infection or of poor renal function, it frequently is necessary to change this to twenty or thirty cc. during the first few days of hospitalization. Likewise, in some instances, it is necessary to administer ammonium chloride in enteric coated tablets to reduce the pH of the urine to a point from 4.9 to 5.2. Since acetone, diacetic acid or beta-oxybutyric acid are not present in the urine, the patient can be maintained on this diet for a considerable period of time.

The patient also is taught to make his own pH determinations which are done one-half hour before lunch in order to avoid the effect of the alkaline tide. A simple and inexpensive apparatus* may be purchased which gives a result of sufficient accuracy that it can be used to follow the patient's progress and to determine whether his diet must be altered or the medication must be increased to maintain the desired pH.

If the pH of the urine remains at the desired level for a period from five to six days, the patient is discharged from the hospital and told to report the daily pH determination to the family physician every two weeks.

I now have six patients in whom I was unable to reduce the pH of the urine below 6.8 or 7.0. In all six of these patients, large bilateral stones, very poor kidney function and a proteus infection were present. In spite of an excess acid-ash of twenty-eight to thirty cc. and forty grains of ammonium chloride daily by mouth, I was unable to reduce the pH to the desired level during the patient's stay in the hospital. In four instances, however, between three and five weeks after the patient was discharged, the pH gradually was reduced to approximately 5.2. All these patients had been treated elsewhere previously with the ketogenic diet by excellent men and the pH had not been reduced to the acid side in any of them.

The following cases are a few in which satisfactory results have been secured by the use of the high vitamin A acid-ash diet.

CASE 1: The patient was a woman, fifty-two years of age, who had large bilateral renal calculi. In spite of marked kidney damage, she was able to carry on her daily duties and the blood urea was forty-five mg. per hundred cubic centimeters. When I first saw this patient, seven and one-half months ago, a stone had never been passed. Since that time, she has followed the diet and more than 273 small calculi have been passed. It is interesting to note that these patients have very little discomfort when the calculi, which resemble a jelly-like mass, are passed. If however, this mass is allowed to stand on filter paper and dehydration occurs, a small accumulation of sand and stone is found. When this patient was last seen, a roentgenogram revealed a marked decrease in the size of the calculi.

*This may be purchased from the LaMotte Chemical Products Company, Baltimore, Md.

CASE 2: The patient was a man fifty-two years of age whose condition had been diagnosed as arthritis before he entered the Clinic.

A plain roentgenogram showed that a large stone filled the entire right kidney. Operation was advised but the patient refused. The high vitamin A acid-ash was prescribed and five and one-half months later, more than 300 small calculi had been passed. While the stone was undergoing solution roentgen examination revealed the breaking up of the solid mass until it was decreased in size by at least fifty per cent. Unfortunately, at this time, the patient was killed in an automobile accident and we were unable to secure the kidney for examination.

CASE 3: The patient was a young girl who had a small stone at the ureteropelvic junction. Inasmuch as she did not wish to discontinue her school work, nonoperative treatment was advised. I was able to dislodge the stone with a ureteral catheter causing it to fall back into the kidney pelvis.

The high vitamin A acid-ash diet was followed and in a period of five and one-half months, the stone disappeared entirely.

CASE 4: The patient was a physician who had two recurrent stones in the right kidney. One stone produced a definite obstruction and operation was advised. However, two previous operations had been performed on this kidney and any further surgical procedure was refused.

The high vitamin A acid-ash diet was prescribed and three and one-half months later, the large stone in the lower calyx of the kidney had entirely disappeared, and the stone in the pelvis of the kidney was definitely smaller.

CASE 5: This patient was a physician also.

A plain roentgenogram revealed nine stones in the left kidney. The high vitamin A acid-ash diet was followed for seven and one-half months and the stones disappeared entirely.

CONCLUSIONS

The following results have been secured by the use of the high vitamin A acid-ash diet in the treatment of urinary calculi.

1. We now have collected a series of twenty-three cases in which stones which were too large to pass spontaneously from the kidney have undergone complete solution as indicated by radiographic studies and by pyelography.

2. We have a group of seventeen patients who passed calculi at frequent intervals. After the high vitamin A acid-ash diet had been followed, all have been entirely free from symptoms for more than two years.

3. During the past two and one-half years, we have had only one instance of recurrent stone formation following operative removal of stones from the upper urinary tract. In this case, the patient did not follow the routine that was outlined for him. I do not wish to infer that postoperatively we only use the high vitamin A acid-ash diet. This is prescribed in addition to the other therapeutic measures that we always have used such as eradication of infection and elimination of stasis. Since this régime has been used the incidence of recurrent stone formation has been reduced from 16.4 to 4.7 per cent in our cases.

4. We also have a series of cases in which the stones have diminished in size, but insufficient time has elapsed to warrant their complete solution.

5. In other cases, we have been unable as yet to note any decrease in the size of the calculi although the patients have followed the diet for a period of from four to five months. It is impossible to determine whether a noticeable decrease in the size of stones will occur after the diet has been followed for longer periods of time. We do believe, however, that if the stone is not producing definite renal damage, and is not disabling the patient from pain, conservative treatment should be attempted.

6. We are quite certain that, if in addition to the other therapeutic measures which have been used previously, a carefully planned diet is prescribed to which vitamin A is added postoperatively, the recurrent formation of stones can be reduced to a minimum.

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DISCUSSION

DR. FLETCHER H. COLBY: I want to congratulate Dr. Higgins very highly on his presentation and his subject which shows, whether you believe it or not, that a great deal of hard and progressive work has been done. There are certain questions that are not clear to me. First, we find stone formation in this part of the country and it is very difficult for us to believe that the average patient is deficient in vitamins of any sort. That, I believe, applies to the average ward patient that we have in our hospitals. Certainly, it would seem to apply to the private patients that we have. If there is no vitamin deficiency, it is difficult to see how feeding vitamin A is going to affect the stones.

Another point is this: in the cases of stones that have resulted from parathyroid disease, we have found at the Massachusetts General Hospital, all these patients have been carefully observed following the removal of the parathyroid tumor to see if there would be any effect on the stone, if the stone would get smaller or possibly dissolve in the spectacular manner that some of these cases we have seen tonight have. In the few instances in which that was done, where the patients were observed, no change, so far as I know, was present or could be determined in the structure of the stone itself. Here is an instance where the etiological factor has been removed, definitely metabolic in character, and I think it would be fair to assume that there might be some change in these patients' stones.

I have enjoyed Dr. Higgins' paper very much and want to thank him a great deal for coming on and talking to us.

DR. E. GRANVILLE CRABTREE: I have a patient who has a series of mishaps, the first of which was an overdose of radium affecting the bladder and rectum, as a result of which I implanted the ureters. One of these resulted in a nephrectomy because it

had to be planted in an unusual place as I could not approach the sigmoid because of extensive adhesions from previous operations. She has lived with one kidney which has functioned perfectly well for nine years. Beginning six months ago there was a change in this patient. She began to have loss of weight, pain, and an intravenous pyelogram showed a great degree of dilatation of the ureter far down to its insertion into the sigmoid. In addition to that, it showed stones in the kidney pelvis. The kidney pelvis was opened and a mass of soft stones, the analysis of which has not yet been completed, was removed. The kidney was placed on nephrotomy drainage as a temporary measure, after demonstrating that the junction between the ureter and the sigmoid was perfectly normal and would admit a large sized bougie. Our difficulty, however, has been the question of persistent alkaline urine on that side as tested by the urinary flow from the catheter drain in her kidney. The infection is a proteus and I was hoping to get some help from Dr. Higgins about acidifying this urine as we have been unable to do it by any measures so far employed.

DR. ALFRED SHOHL: I came here to listen and to learn. By no stretch of the imagination can I be considered a urologist. Dr. Deming tried to teach me some things about urology once but I am afraid it didn't take. I was associated with him once in an attempt to modify the acidity of the urine in various ways. Perhaps he will tell you about the methods you can employ best in changing the acidity of the urine and what results to expect.

Speaking as a chemist, there is no question that uric acid is soluble to alkalies. As far as the cystine oxalates are concerned, the most acid urine one can obtain would be approximately the condition for the precipitation of cystine.

I am naturally very much interested in the question of vitamin A deficiency in relation to stone formation and very often I have seen these calculi in rats. I have no doubt that the acidity of urine can be influenced by the diet but I am still in doubt, however, as to how much importance one must lay to the acidity factor and how much to the vitamin A. As far as I know, vitamin A deficiency in human beings is not widespread, at least in this country but where vitamin A deficiency occurs it is not invariably associated with calculi.

On the question of measurement of the acidity of the urine by the colorimeter, I agree with Dr. Higgins. With hundreds of determinations, so far as I know, no practical difference has been made out in any type of urine between the electrometric and the colorimetric measures. It is true that there is a definite salt effect on the indicators, but I do not think that is ordinarily of sufficient magnitude to vitiate any result that may be determined by colorimetric determinations of the urine. I think Dr. Albright's ideas with regard to phosphate are well taken and any attempt to acidify the urine by phosphates is perhaps a step in the wrong direction.

I would like to ask Dr. Higgins the diets with which he produced pure calcium carbonate stones in rats.

DR. E. L. PEIRSON: I would like to know what happens to stones in rats if they are put on an acid diet without vitamin A at all.

DR. ROBERT R. BALDRIDGE: I would like to ask Dr. Higgins whether the dissolving of stones, in cases where infection was present, had any effect on the infection, whether the infection persisted or not.

DR. THOMAS N. HEPBURN: I have known of Dr. Higgins' excellent work by his published papers, and I came up from Hartford to hear it personally presented, because I thought it of such value. Also I wished to see his pictures of dissolving kidney stones, certainly a most dramatic presentation. I have been equally charmed by the convincing work the group in Boston has done at the Massachusetts General Hospital on disturbed metabolism as a result of hyperparathyroidism.

For a number of years, I have removed stones from the kidneys and I am astonished at my good fortune that so many of them have not recurred. I recall twenty-five or thirty years ago, when dietary treatment for the prevention of stones was a prevalent medical concept. I remember the uncertainty which many of us felt who were conscious of our ignorance of the metabolic processes involved. I remember how we were told some stones would form with acid urine and some with alkaline urine. Naturally there was a revolt by my generation against accepting such poorly proved theories.

Now shall we accept as proved these more recent theories? We must keep in mind that a large proportion of stones are unilateral, and that without resorting to any complicated metabolic diet or parathyroidectomy at least sixty per cent of our stones do not recur. Is concentrating the attention of the poor human stone victim on the fact that he may reform stones, good treatment, when sixty per cent go along rather happily without recurrence? I have felt and feel now my gross ignorance on this subject, my incapacity to judge except in a relatively small group, which stones are metabolic and which stones are the result of dietary deficiency. I hope that as a result of this work, urologists will better understand the etiology and treatment of kidney stones resulting from dietary or glandular errors. I also hope that the minds of urologists will not be so centered on the complex phases of this lesser group that they will make all their patients too stone-conscious, unless they are quite sure to which group of stone makers they belong.

One thing has not been mentioned, to which attention should be paid and that is the value of good drainage of the kidneys at the time of operation, and to the value of forcing fluids where you are uncertain as to what the etiology of the stone is. Those of us who are not fortunate enough to have metabolic laboratories at our command, and are afflicted with a stubborn skepticism will do well if we keep the urine very dilute with forced fluids and be sure at the time of the operation that there is not some obstruction, even of a mild character. Adequate kidney drainage is still probably the best corrective for renal infection. Remember that the majority of these patients will not reform stones and they should not have to carry in their minds always the feeling that they are handicapped by having to stick to special diets, and probably only a very small group should be trained to examine their urine frequently, as diabetics do, and so become always conscious of their disability.

I do not wish to convey the impression that I am not properly grateful and appreciative of the very splendid work that is being done by our metabolic chemists and by our food experts. I speak only for the encouragement of urologists who are not clear in their minds regarding this complicated process, and for the benefit of the morale of the majority of those human beings who have had or will suffer from a kidney stone.

DR. CLYDE L. DEMING: I would like to ask Dr. Higgins two questions. It is considered that viosterol is having somewhat the opposite effect from vitamin A, that is cod liver oil, and I wonder if Dr. Higgins has seen any stone formations in orthopedic

cases that have had viosterol. In using his acid-ash diet, does he follow pretty closely the diet as outlined by Dr. Keezer?

DR. C. C. HIGGINS: Of course, the discussion of the etiologic factors involved in the formation of urinary calculi could be prolonged indefinitely. Probably no single factor is instrumental in the production of all stones; however, by our experimental work in vitamin A deficiency, conditions are produced which explain satisfactorily the mechanism of calculous formation. There is likewise no doubt but that hyperparathyroidism is associated with the formation of calculi in some instances.

In the series of cases of urinary calculi that I have studied, I have not noted a single case associated with hyperparathyroidism and the blood calcium and phosphorus determinations always have been within normal limits. We have operated upon three parathyroid tumors, however, which were associated with hyperparathyroidism and in which there were no evidences of calculi.

In a communication with Dr. Max Ballin of Detroit, he told me that in the cases which he reported, in no instance were urinary calculi found. If cystoscopic examination is performed on a female dog every three or four days, and the region just in front of the trigone is traumatized with a wire, an ulceration is produced. If the urine of the dog then is rendered strongly alkaline, you will notice a deposition of phosphates on the ulcerated surface which becomes further united by the fibrin which exudes from the raw surface. If this deposit then drops into the base of the bladder and the alkalinity of the urine is continued, the gradual development of a calculus can be followed.

The question has been asked as to whether vitamin A deficiency is a common clinical finding. It is a very simple matter to make a diagnosis of extreme avitaminosis. However, in many cases, it is difficult to determine whether a mild degree of deficiency is present. After all, you cannot overlook the statistics of Jeans which were published in the *Journal of the American Medical Association* a short time ago. He found that approximately twenty per cent of the children who entered the dispensary of Iowa State University for diagnosis and treatment were deficient in vitamin A. Obviously, if a marked degree of avitaminosis is present, the condition is recognized and treatment is instituted. Therefore, for the production of urinary calculi, both in patients and in experimental animals, only a very mild degree of deficiency must exist over a long period of time.

The question is asked, how much vitamin A do we secure in our food? The usual food sources of vitamin A are milk, butter, eggs and green vegetables. The vitamin A value of animal foodstuffs varies considerably with the diet of the animal. This is especially true of dairy products such as milk, cream, butter and eggs. The Ohio State Experimental Station has found that when cows are on winter feeding, some milk contains less than half as much vitamin A as when the cows are on summer feeding in pasture. Thus the variation in vitamin A content of dairy products is markedly affected. Likewise, eggs toward the end of the laying season frequently contain only half the vitamin A content that they do in the earlier part of the year. Of course, carrots contain a large amount of vitamin A, but unfortunately, people are not especially fond of them.

With regard to the action of viosterol: About two years ago, we started working on the effect of viosterol in rats to ascertain whether calculi could be produced. In ten of fifty experimental animals, calcification was found in the renal parenchyma; however, no calculi were evident. In view of other experimental work that has been done, I do not feel that preparations which contain viosterol should be utilized over a long period of time. As stated previously, the stones which first formed experimentally in the white rat were composed of calcium magnesium phosphate with traces of carbonates. No oxalates or uric acid were present. We found later that by decreasing the phosphorus in the diet in relation to the calcium, a reversal in the chemistry of the stones occurred. Now they were composed chiefly of calcium carbonate with only traces of phosphates.

Is the alkalinity of the urine the chief factor in the production of stones? When the white rats are maintained on a diet deficient in vitamin A, the urine becomes alkaline. If, however, small amounts of ammonium chloride are given and the urine remains approximately neutral, calculi can be produced but it requires a longer period of time. After the stones have been formed experimentally, acidifying the urine alone does not cause a solution of the stone. Likewise you cannot prevent the recurrence of calculous formation due to the fact that the lesions in the mucosa of the genito-urinary tract are still present. We know that vitamin A has a specific effect on the epithelium and is a most useful medication to promote its healing.

In the work reported on calculi associated with hyperparathyroidism, the point that has interested me is that the calculi were phosphatic in type and were produced in an alkaline urine. I am waiting anxiously to see such a patient to determine whether by the use of the high vitamin A acid-ash diet alone, a solution of the stone can be accomplished before operation is performed on the parathyroid glands, or whether a positive Jeans' test is present. The clinical findings in these cases, that is, the phosphatic stones and the alkaline urine, are similar to those which we made in our dietary work. It may be true that the LaMotte apparatus does not give an absolutely accurate determination of the pH of the urine; however, it is sufficiently accurate to warrant its adoption to follow the progress of these patients. As we follow the progress of a patient with diabetes by a blood sugar examination, likewise we follow the progress of patients on the high vitamin A acid-ash diet by a pH determination of the urine.

The effect of diet on infection: A short time ago in St. Louis at the meeting of the Southwestern Branch of the American Urological Association, I was asked if I had noticed that in many instances the renal infection had subsided after the patient had been on the high vitamin A acid-ash diet for a period of time. I noticed that in a few cases, but did not pay a great deal of attention to it. It has been stated that the bactericidal effect of the urine on a patient who is following the ketogenic diet is due to the beta-oxybutyric acid. This, of course, is not present in the urine of the patient on the high vitamin A acid-ash diet. If the urine has bactericidal properties, therefore, it must be due to the fact that the pH of the urine is at a level which is not favorable for the growth of bacteria and is maintained at this level for a considerable period of time.

I will not go into detail about the discussion of the cystine stones. They are rather unusual. However, I feel certain that a cystine calculus can be formed experimentally just as easily as a phosphatic stone if we can produce a constant cystinuria for a long period of time and maintain the experimental animal on a vitamin A deficiency diet. Likewise, I believe an oxalate stone can be produced experimentally if we can produce an oxaluria in an experimental animal for a considerable period of time and maintain it on a diet deficient in vitamin A.

MASSACHUSETTS MEDICO-LEGAL SOCIETY

A REVIEW OF THE VARIETY OF POISONS WHICH HAVE CAUSED DEATH IN THE MASSACHUSETTS STATE HOSPITALS FOR MENTAL DISEASE*

BY ANNA M. ALLEN, M.D.†

DURING the twenty years, from 1914 to 1934, which this review covers, the number of deaths caused by poisoning (exclusive of alcohol) in the State Hospital of Massachusetts for mental diseases reaches the surprisingly low figure of forty-one; in twenty-two of these cases the poison was ingested before admission. The hospitals' population is between 22,000-24,000 patients. In this period there were approximately 2,600 cases which came under the jurisdiction of the Medical Examiner, thus giving us a figure of somewhat over 1.5 per cent for the incidence of poisoning in the sudden or unexpected deaths in the forty-one cases.

As can be seen from the accompanying table, the poisons fall into a great variety of categories.

Corrosive poisons	Lye	4 cases
Non-metallic poisons	Iodine	2
	Phosphorus	1
	Fluorine	1
Metallic poisons	Arsenic	7
	Mercury	4
	Lead	2
	Antimony	1
Gaseous poisons	Carbon Monoxide	4
Alkaloidal poisons	Morphine	2
	Nicotine	1
Non-alkaloidal organic poisons	Cresols	4
	Phenols	3
	Phenobarbital	3
	Cyanide	1
	Tri-ortho-cresyl-phosphate	1

Of the corrosive poisons, lye is easily accessible used as it is, so frequently in kitchen work. All of the four deaths caused by this substance were suicidal. The most rapid of these deaths occurred thirteen hours after ingestion of the lye and postmortem examination showed an intense hemorrhagic necrosis of the gastrointestinal tract, including the mucosa of the mouth, esophagus, stomach and extending a few feet into the small intestine. There were several perforations in the esophagus and stomach. It was not possible to determine the exact amount taken by this patient, but in the case of another patient who died in thirty-nine days, it was estimated that one ounce of lye was consumed.

Tincture of Iodine caused death in two individuals. A seventy year old woman drank approximately three and one half ounces, became very cyanosed, and died in one hour. Autopsy showed edema of the glottis and necrosis of the gastric mucosa.

Phosphorus in the form of a tube of Bisnit Rat poison was spread on chocolate and consumed by a twenty-four year old male who felt guilty over an illicit love affair. He suffered from nausea and epigastric pain, and died in thirty-one hours. Autopsy showed pulmonary edema and congestion, necrosis of the epithelium of the esophagus and a characteristic odor from the abdominal cavity.

An accidental death occurred in one hospital when roach powder, a mixture of sodium fluoride and sodium silicofluoride, was mistaken for powdered sugar and used in making hard sauce to go with the noontime dessert. The patient who was mixing the sauce, tasted it on several occasions, and then complained of weakness and nausea. He vomited copiously and lapsed into a state of mild shock, which responded well to treatment, though generalized weakness and muscular cramps continued. Some five hours later he complained of dyspnea, and expired almost immediately. Autopsy showed subpleural and epicardial hemorrhages, as well as extravasations of blood into the lung tissue and intense hyperemia of the kidneys. The blood was liquid throughout and when examined for calcium by Mr. E. H. Stotz, Dept. of Biochemistry, Harvard Medical School, it contained only 5.8 mg./100 cc., instead of the normal 10 mg./100 cc.—the tetany level is approximately 7 mg./100 cc. Dr. William F. Boos, toxicologist, found fluorides present in all the organs, as well as in the heart's blood. In this case death was presumably due to an artificial tetany brought about by the fluoride combining with the blood calcium to form a calcium fluoride which is of extremely low solubility. Since this fatality, all the roach powder used in the Massachusetts State Hospitals for Mental Disease is colored so that a similar mistake will not recur.

Of the Metallic Poisons, arsenic caused the most deaths—seven fatalities. In this group, however, are listed four cases who died while undergoing treatment for syphilis; two of these were caused by the administration of un-

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neutralized arsphenamine, and two died shortly after an injection of sulpharsphenamine, presumably because of an idiosyncrasy for this substance. The other three deaths were suicidal and the arsenic was taken before admission to the mental hospital. It was ingested in the form of Paris green (copper acetoarsenite). A sixty-eight year old man took six tablespoonfuls of Paris green, mixed it with milk, and drank it. He lapsed into a state of shock, later became cyanotic, and died five hours and twenty minutes after taking the poison. At autopsy there were numerous particles of bright green material in the stomach. The mucosa of the stomach was swollen and hemorrhagic. Subpleural and subepicardial hemorrhages were common.

Mercury, in the form of bichloride tablets, caused death in three cases. A depressed male patient, whose wife had taken him on visit from the hospital against advice, took six tablets. He lived eight days with almost complete suppression of urine. Another patient smuggled in some tablets of bichloride of mercury, after returning from a visit to her home. She ate several and died three and one-half days later. Autopsy showed hemorrhages into the mucosa of the stomach, ileum and colon, as well as an acute toxic nephritis. A forty-two year old patient suffering from the effects of chronic alcoholism drank approximately three ounces of a 5 per cent solution of mercurochrome. He died forty days later. Autopsy showed pulmonary tuberculosis, also an acute nephritis. The skin of the body was pinkish-white and definite pink staining was noted in the lungs, liver and bladder.

Two cases of occupational lead poisoning developed psychoses, and died in State Mental Hospitals with the usual syndrome of generalized intoxication.

Antimony Trichloride was used as a means of suicide in the case of a thirty-five year old cabinet worker. He drank about 40 cc. of paint remover containing butter of antimony and suffered from severe pain in the throat and epigastrium. He died in twenty hours. Autopsy permission was refused but a quantity of spinal fluid was removed at the suggestion of Dr. Myrtelle M. Canavan, and this when tested by Dr. William F. Boos, toxicologist, was found to contain antimony; the first time antimony has been recovered from the spinal fluid.

Deaths from gaseous poisons numbered four; all of which were suicidal attempts before admission and in which death was caused by carbon monoxide. Illuminating gas was the method employed in three cases, and the gas from the exhaust of an automobile engine in the fourth case. This latter mode was used by a twenty-four year old male, who died in fifteen hours. No autopsy was performed on any of these cases.

Of the deaths from alkaloidal poisons, it was questionable whether morphine was the prime agent in the two listed as such. It was known that both of these patients had used this drug for some time before admission, but the manner of death and the signs before death were not conclusive. There was a probability of poisonous alcohol being a factor in the death of one of these, and organic heart disease was definitely diagnosed in the other.

Nicotine caused death within fifteen minutes in the case of a forty year old man who drank an unknown quantity of an insecticide containing this alkaloid. He developed convulsions, frothed at the mouth, became rapidly cyanosed, and died. Autopsy showed the blood, fluid throughout, and the stomach contained a green liquid with a heavy precipitate and characteristic odor.

Under the non-alkaloidal organic poisons are listed four cases of suicide due to cresols, creolin 2, lysol 1 and sulphonaphthol 1. A thirty-eight year old woman drank approximately seven ounces of creolin. She died in two days. The other creolin poisoning case consumed an unknown quantity and lived six days, showing at autopsy acute gastritis, nephritis and bronchopneumonia. A twenty-three year old syphilitic woman drank the contents of a three-ounce bottle labelled Lysol. She was unconscious within a few minutes, showed signs of pulmonary edema, and died within one hour. The sixty-one year old widow who drank sulphonaphthol had also cut her left wrist, and throat from ear to ear. She lived for four days.

Phenol was taken in the form of carbolic acid by a forty-eight year old man, who died fifteen minutes after it was discovered that he had taken the poison. Six to eight ounces of an insecticide containing phenol and kerosene was drunk by a 50 year old woman. She became cyanosed and comatose, dying within six hours of drinking the fluid. Indelible ink which contained phenol was taken by an insane woman, who died one hour and forty minutes later.

Phenobarbital or Luminal caused three deaths. In two of these approximately seventy-two grains were administered in mistake for magnesium sulphate. Deep coma resulted and a rise in temperature, as high as 105°F. Pulse and respirations were also markedly increased in rate, and there was evidence of pulmonary edema. One man died in fifty-four hours, the other in sixty-four hours. The other death from luminal was suicidal. It occurred in an epileptic girl who took an unknown quantity and was found unconscious. She received drastic treatment but remained inert until her death some sixty hours after taking the drug. Autopsy showed little of note, except pulmonary edema, an enlarged liver (2175 grams), congested kidneys and slight subarachnoid oozing of blood.

Sodium Cyanide, the amount unknown, ingested with suicidal intent, caused death in a twenty-five year old chemical engineer, who had

voluntarily come to a State Hospital after his mother committed suicide. He died within ten minutes after taking this poison. Sodium cyanide crystals were found in his clothes. Autopsy, confined to the stomach only, showed the mucous membrane of this organ to be bright red and velvety.

Tri-ortho-cresyl-phosphate or so-called jamaica ginger was presumably partly responsible for the death of a seventy-two year old male, who also suffered from chronic alcoholism. He had an advanced polyneuritis on admission to the Mental Hospital, but he did not die until one and one-half years later. At autopsy, the spinal cord showed atrophy of the grey matter and anterior horn gliosis.

Of these forty-one deaths caused by poisoning, twelve were accidental and twenty-nine suicidal. The accidental deaths may be listed as follows:

Antisyphilitic treatment	4
Lead Poisoning	2
Luminal	2
Morphine	2
Sodium Fluoride (roach powder)	1
Jamaica Ginger (Tri-ortho-cresyl-phosphate)	1

It is difficult to see how the majority of these can be completely prevented. Those that occurred before admission (lead poisoning, morphine and jamaica ginger) are outside our influence. Of the remainder, the luminal deaths were caused by an error which is unlikely to recur, for the reason that the bottles which contain the magnesium sulphate and luminal have no longer any similarity and cannot be mistaken for each other. The roach powder is tinted so that there is now a distinct difference between it and powdered sugar. Two of the fatalities in giving the treatment for syphilis, those due to the administration of unneutralized arsphenamine, are guarded against recurrence by the fact that it has been replaced by sulpharsphenamine and neoarsphenamine. The other two deaths, which occurred after the injection of sulpharsphenamine, were unavoidable in that there was no obvious contraindication for the use of this therapeutic agent.

The suicides were all caused by poisons which are easily accessible and for the most part may be bought at any drug store. Insecticides, antiseptics or disinfectants being employed by many people require no ingenuity in obtaining them outside of the hospital. Within the hospital, many ruses were employed by the depressed patients to obtain these poisons. Occasionally they were smuggled in after the patient returned from visit. Tincture of iodine was stolen from the surgery by a patient polishing the floor at the same time as a nurse was in the room attending to another patient. With regard to the indelible ink, it was not known beforehand that this contained phenol, and the bottle was not marked poison. In the case of two of the suicides, luminal and sodium cyanide, even after careful investigation it was not possible to determine just how the patients obtained them. The insecticide containing nicotine was taken from the greenhouse, while the florist was absent for a few minutes, by a patient who had been mowing the grass outside. The majority of these patients had shown no suicidal intent previously and several appeared well enough to be allowed parole of the grounds.

When classified according to the mental state, we get the following result:

Undiagnosed	13
Alcoholic	6
Manic Depressive-Depressed	5
Dementia Praecox	4
Toxic Psychosis	4
Psychosis with Psychopathic Personality	2
General Paralysis of the Insane	2
Psychosis with Mental Deficiency	2
Traumatic Psychosis	1
Psychosis with Syphilis	1
Psychosis with Epilepsy	1
Total	41

The thirteen cases that were undiagnosed had taken the poison before admission to the hospital and died before an accurate diagnosis could be made. The alcoholic group is surprisingly high, but may be accounted for by the depressant effects which frequently follow alcoholism. The manic depressive figure, when compared with that of dementia praecox, is high considering that the latter form a much higher percentage of the State Hospital population than the former.

A brief analysis of the age at death shows that twenty-eight of the forty-one were under forty years of age at death. The youngest to commit suicide was twenty-one years of age and the oldest was aged eighty-four years. With regard to sex, seventeen were female and twenty-four male.

CONCLUSIONS

1) Massachusetts has cared for 22,000-24,000 mental patients yearly, for twenty years.
2) Approximately 2600 cases have come under medical examiners' attention at their death in that time.
3) Only forty-one or slightly over 1.5 per cent of this number have come to their death by poisons.
4) Twelve of the forty-one, were accidental, twenty-nine suicidal.
5) Twenty-two of the forty-one had imbibed the poison before coming to the hospital; nineteen after coming to it.
6) The poisons were various; corrosive, non-metallic, metallic, gaseous, alkaloidal and non-alkaloidal organic poisons; metallic poisons were in greatest number.

7) The mental diagnoses ranged from "undiagnosed" (13) to psychosis with epilepsy (1).

8) The ages were twenty-one to eighty-four.

9) Males twenty-four, females seventeen in number.

10) Steps have been taken to minimize these deaths.

DISCUSSION

DR. WINFRED OVERHOLSER: I am sorry that I did not hear the whole of this presentation, I know something of it, naturally. We are very much interested in the office of the Department in the sudden deaths that occur in our hospitals, particularly by suicidal intent.

One thought that occurs to me in looking over the summary on the board is that it is quite obvious, I think, that even under close supervision, such as patients have in mental hospitals, it is not possible to guarantee that there will not be suicidal deaths.

One thing that impresses me, too, in the outside cases, and I am sure it impressed the others here because you are all called in cases of this sort, is the great danger, in cases of depression, that there will be an attempted suicide, which, all too frequently, is successful.

The seriousness, too, of depressions occurring in patients who are in their homes is not sufficiently recognized. We know that. Of course, it is common knowledge from reading the papers, and it is also common knowledge to all of you gentlemen who are called to view the bodies.

The type of poisoning that particularly attracted our attention, recently, is that by sodium fluoride, which I imagine Dr. Allen took up in some detail; the ingestion of roach powder. As a result of this affair being called to our attention, we changed the formula by adding a small amount of lamp-black, so that the cockroach powder used now, with this formula, is off the white color and is, therefore, sufficiently different in appearance from the powdered sugar so that at least we hope this mistake will not be made again.

Dr. Barrett, the Assistant Commissioner, is present, Dr. Gay, and it may be that he has something that will be of interest to the group.

DR. BARRETT: *Dr. Gay, and Members*—The thing that is especially interesting to me in discussion of suicide in the State Hospitals reverts to a consideration of administration. It, oftentimes, is an administrative problem that is very difficult to cope with. We do have accidental deaths from poisoning in institutions, and some in which the patients are very strongly implicated. There are others, some of which Dr. Allen has reported here, where the patient was not active in the process at all, especially the luminal deaths, in which there was another personality factor involved.

We take very special precautions in the allocation of medicines on the wards, which is absolutely necessary. We must have medications available for immediate use on various types of hospital wards. That is an improvement, I think, over the old hospital system where all medications were disbursed from a pharmacy, by doses. Under those conditions, oftentimes the patient got medications that had been ordered for them, and oftentimes they didn't, and when they did get them, they were maybe two or three hours late and they didn't get the required dosage.

Under the State Hospital system of Massachusetts, I would like to say that we more or less pride ourselves that we are actually conducting hospitals and not asylums. We are trying to make treatment for patients available at all times so that it is necessary to have medications in certain quantities on the wards. We have taken precautions to see that these storage places are under at least a double lock, and that they are available only to persons who are authorized to administer these medications on order of physician. But, it seems that sometimes there is an error on the part of the administering person. Sometimes there will be that personal factor of becoming somewhat careless and leaving things out. Whether that can ever be entirely corrected, I don't know. I seriously doubt it.

The case of sodium fluoride poisoning, I think, is one of special interest in that the way this was administered is something exceptional and new to me. I had never even suspected that this mixture might be stored in close proximity to powdered sugar. But, that is another personal equation, I imagine, and the Department is especially concerned in seeing that a minimum of those cases occur. I thank you.

PRESIDENT GAY: Thank you very much, Dr. Barrett. Is there any further discussion?

DR. MAGRATH: I wish to congratulate Dr. Allen on the presenting of such an enlightening and complete analytical study of causes of death from poisoning among institutional workers. It has been very enlightening to know what your experience has been in the State institutions.

My own experience is with people who are, for the most part, in the open, and, as we see, they take matters into their own hands; when this happens, they take almost any of the things listed on the board here.

As I look them over, the substances enumerated include only one, nicotine, with which I have not had experience. I congratulate the chemist on getting nicotine. It is a difficult thing to do.

It is a wonder that more accidental deaths do not occur incident to the compounding of prescriptions. Accidents do occur, of course, but in proportion to the number of prescriptions filled, they are quite rare.

One comes to my mind where a North End druggist or his clerk, who is not a registered pharmacist, by the way, dispensed on a prescription something which the purchaser of the medicine took home and then ingested, and she very speedily went into convulsions and died. What the physician had written for was stypticin. She suffered from menorrhagia, and the druggist's clerk read it as "strychnine". He reached up on the shelf and took down a bottle of strychnine sulphate from among the poisons, and put up the prescription in terms of a strychnine instead of stypticin.

It isn't to be wondered at that the poor lady died and died promptly.

In another instance of what we might call the pharmacy accidental type came the demise of a woman who bought, or thought she bought, citrate of magnesium, effervescent citrate of magnesium, of which she took an appropriate amount and thereafter became unconscious and vomited, and very speedily died. That was a case of poisoning and it was difficult to trace the source of the error, but probably it was outside of the pharmacy, because the pharmacist showed me the package from which he had taken the materials in order to prepare this

bottle of medicine. It evidently took place in the factory, or at any rate on the premises where the cartons were put up. It was a mislabeled package, instead of containing citrate of magnesia, it contained tartar emetic so that there was a mistake, not on the part of the pharmacist, but on the part of the wholesaler who manufactured it.

This paper of Dr. Allen's was very enlightening, and I am very grateful to have had the opportunity to hear it.

A CLINICAL LECTURE ON MIGRAINE*

BY A. H. GORDON, M.D.†

THE object of my talk this evening is to present the salient features of *Migraine* from the standpoint of the clinician, and to emphasize the width of the many gaps in our knowledge of this mysterious ailment rather than the few small fragments of what we think we know.

Having once about ten years ago been emboldened to write on the subject of migraine I referred to that article when called upon on this occasion, and find I can give whole-hearted consent to at least one paragraph which says, "For the purpose of this discussion, by migrainous headache we mean a headache, prostrating in intensity, paroxysmal in onset and periodical in recurrence, which can turn a strong man into a worm and make the affections of a woman dark as Erebus, which may pass a legacy from generation to generation and which attacks a girl as she approaches womanhood and is said to leave her at the menopause but frequently doesn't."

At the outset one must ask the very reasonable question: Is there such a disease as migraine? And immediately I hear twelve good men and true in this room answer, "Yes, for I have it." But again I may ask, Is the migraine that afflicts any one of you twelve the same as that which afflicts the other eleven? These two questions cannot be answered with certainty for we are still compelled to identify the disease by the clinical features which it possesses, rather than by the morbid anatomy which it does not possess, and our attitude toward it must for the present be one of rational empiricism.

There is much evidence that this symptom complex of migraine was recognized by the physician of the early days of the Christian era and in particular its tendency to attack one side of the head is remembered in the early name hemicrania, which in French became migraine and which later in English was corrupted to megrims and this again was applied somewhat disdainfully to any sickness which could be brought on at will to avoid a worse alternative.

Before we touch upon what we are to do for migraine, a word should be said about what migraine does to us, I mean to us as clinicians. For it becomes a mirror into which the doctor may look and see what manner of man he is.

We have heard much these late years of the forgotten man, and here we find the forgotten disease, for how often on the eruption of its headache or its vomiting into our peace of mind is the isolated event regarded as an "acute indigestion" (whatever that is) or as a "toxic manifestation" (whatever that is) or as a "neuralgia" (whatever that is) without the effort to integrate the symptoms into a clinical whole by relating them with forgotten or misunderstood episodes in the past.

If we are of the school to which focal infection explains everything, our eyes stray, not unerringly but automatically, to the teeth or the tonsils until Moloch is appeased, or if we are true materialists, a suspicious tenderness is eventually found over the gall bladder or appendix and that's that; and, if, perchance we are gifted with an imagination, and no good clinician is without it, the symptom complex of migraine leaps quickly to our minds, and by painting the history here and pruning it there, a good case for the neurological picture of true migraine can be made from a chronic nephritis, a cholecystitis or a pyloric obstruction.

Just here we should pull ourselves together and decide what we mean to include within the limits of the term migraine. In a disease without a morbid anatomy one man has almost as much right to include in the picture any sort of recurring nausea or dizziness or what not, unassociated with a typical attack, as another has to exclude recurring headaches which are associated with well-defined local paralyses; but until we know more about the classical disease than we do now, it is wiser not to call anything migraine that does not measure up to the orthodox description of a periodical headache, chiefly one-sided, which is preceded by certain types of aura and followed by nausea or vomiting, the whole attack being succeeded by a return to normal health.

The approach to a nebulous subject like migraine is buttressed somewhat by figures and these figures help to keep us from losing ourselves in speculations. To make these figures less deceiving I have averaged several groups of statistics and it is fair to say from these that three-fourths of the cases of migraine commence before twenty-five years of age and that one-half show the presence of another case in the same or in the previous generation, and that in addition the cases descend with greater frequency through the maternal side of the family.

Cases occur more frequently in females, some

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would say two and a half times as frequently as in males, but others feel that this disparity is more apparent than real.

City people seem to be more affected than country people.

The clinically important features of migraine may be set down as:

1. Periodicity.
2. Return to normal between attacks.
3. Headache which, in its character of one-sidedness, has given the disease its name of hemicrania or migraine. Always severe, the attacks of headache are often prostrating. Some patients will say that if the house burnt down they could not move, so great is the pain.
4. Nausea and vomiting. These unpleasant symptoms occur in three-quarters of the cases and give to the attack its name of sick headache, but vomiting as a rule does not end the attack. To be classed with nausea and vomiting is a group of other symptoms involving the vegetative nervous system, coldness, giddiness, collapse, pallor, sweating, polyuria and diarrhea, which are of a general character; and unilateral sweating and flushing, and fullness and throbbing of one temporal vessel which point toward a sympathetic involvement on one side.
5. Prodromata are not invariable but are frequent. Languor and malaise followed by giddiness and coldness often precede the headache.
6. Ocular manifestations such as zigzags, spectra and scotomata were found by Elliott in 44 per cent of cases and in the form of hemianopia in 18 per cent. This is a proportion far above that which one sees in ordinary medical consultations. I am inclined to think that from their dramatic character, the ocular symptoms are kept in the foreground and that 10 to 15 per cent would cover the number we ordinarily see.
7. Time of onset. It is quite striking in how many instances the attack commences in the morning on rising. Another feature difficult to explain is that if the attack continues into the second day the sufferer's sleep may be undisturbed in the intervening night. Ordinarily however when sleep occurs the storm blows over.
8. Undoubtedly a feature of true migraine but approaching the border line of diagnostic error is the group of unilateral sensory and sometimes motor symptoms that may develop. These may be numbness of the face, arm or leg, slight weakness and slight aphasia and certainly hemianopia. Ryle reports a group of such cases and in addition one with vestibular symptoms.

Their transient character, their appearance in only the more severe attacks and their absolute disappearance between attacks hold these phenomena within the concept of the disease, but keep us on the "qui vive" lest something may be lurking behind the migraine syndrome. One may take still stronger ground in what is called the ophthalmoplegic type of migraine. In a fairly wide experience with the ailment I have never met with a case. It is described as a migrainous attack in which periodic paralysis of one or more branches of the third nerve may occur and in a few autopsies some organic disease has been found to account for the paralysis.

These features are the ones which commonly make up the clinical picture of migraine but the presence of the ailment in a patient's parent or brother or sister adds as greatly to one's assurance of a correct diagnosis as does its absence inject a feeling of uncertainty.

Having set down what appear to be reasonable clinical criteria for what we shall regard as migraine it is of interest to mention certain cases which for the time may be regarded as inhabiting the border land of this disease. One such is what might be called, whether justly or not time will tell, abdominal migraine. Only one case of this nature has come under my care.

A twelve year old boy had suffered from periodical attacks of abdominal pain with projectile vomiting. These attacks had commenced at four years of age and had continued at intervals of from a few days to one month. They were preceded by lassitude and distaste for food, and came on with severe abdominal pain which continued until a projectile vomiting of large amounts occurred, which gave relief to the pain. The attacks had no relation to food and after they passed off he felt quite well again. He had been operated upon for appendicitis four years before without relief, and when I saw him I suspected a partial obstruction of the small bowel. His x-ray examination and all features of his physical examination were negative and there was no fever, but as he was incapacitated from school and from play an exploratory operation was suggested, which showed absolutely no pathological condition to be present. He recovered rapidly from the operation but was neither better nor worse after it.

The subject of abdominal migraine is a dangerous one to venture upon, dangerous for the physician, but still more so for the surgeon, but I think that there is little doubt that such a condition does exist. An attack of epigastric pain and vomiting without fever, with or without diarrhea, periodical in its appearance, either replacing a cephalic migrainous attack, or appearing in a person who has such attacks, should be carefully weighed and measured before its victim is submitted to abdominal section. I would be the first to admit that a gall bladder or an appendix or a pancreas or a gastric ulcer might be at the bottom of such a symptom complex, but in the light of the case to which I have referred I would be more chary the next time in advising operation.

Another of the borderland types is that associated with psychical symptoms. Neilson reports an instance in a physician of thirty-seven who had periodic attacks of loss of memory and loss of orientation with defects in his visual

field lasting two or three hours and preceded by fortification spectra. One might ask if these attacks were migrainous or epileptiform or whether they were a type of periodic psychosis involving the personality of one who suffered from migraine.

The question has already been raised as to whether the occurrence of definite paralyses of the ocular muscles with attacks of hemicrania could be properly classed as migraine and the same can be said of the facial pareses which have also been reported. The presence in some autopsies of local organic lesions in cases of this type further tends to throw doubt upon their truly migrainous character. W. J. Adie of London reports seven cases of migraine which developed permanent hemianopia and in one of which a subarachnoid hemorrhage developed. He puts forward the observation that in migraine in which a recurrent and temporary cerebral circulatory disturbance occurs, this disturbance at times may be severe enough to lead to cerebral infarction or to subarachnoid hemorrhage. As I have already said, we cannot yet readily include within the concept of migraine instances in which permanent structural damage occurs, but such cases are of use in offering sidelights upon a very obscure problem.

In this connection I have been struck and I have no doubt many of you have been struck by the frequency with which hypertensive vascular disease appears in those who have been in earlier life the subjects of migraine. The association of migraine with the idiopathic convulsive state has also raised a good deal of discussion. Dr. Stanley Cobb has collected a group of 1086 patients with idiopathic convulsive disorders and found in 9139 relatives of these people that forty-three per 10,000 had migraine. In 250 control cases without convulsive attacks their 1896 relatives showed only fifteen per 1000 with migraine. Eely found that in people with convulsive disorders a greater number had ancestors with migraine than had ancestors with the convulsive state. Buchanan's figures give the same result, and he comes to the conclusion that migraine and essential epilepsy are transmitted from generation to generation as the expression of the same underlying factor in the germ plasm. I do not deny the correctness of the figures but no such close affinity between the two diseases has appeared in my own experience.

What are the views at present of the nature of this mysterious malady? Many observers have argued that it is a toxemia, but to put the matter shortly no group of cases has yet given evidence of significant alteration in the blood or urinary chemistry, though an interesting observaton was made by van Leeuwen and Zeidner of a substance found in the alcoholic solution of the blood of asthmatic and migrainous patients which stimulated the smooth muscle of the gut of a cat upon which the blood of controls showed no effect. Diamand, in 1927, in a small group of cases found an increase in the van den Bergh reaction and urobilinogen in cases of migraine but no such findings have appeared in cases under my care.

Others have believed that it is an allergic disease. Vaughan and Balyeat upon investigating patients with migraine have found responses to various foods by intracutaneous injection, and on that basis have treated these patients by removing the offending food. Vaughan has found 70 per cent of cases of paroxysmal headaches to be associated with allergy and has reported relief in 51 per cent of thirty-seven cases, and Balyeat reported 52 per cent relieved of symptoms in fifty-five cases. We all have seen occasional instances in which certain foods as wheat bread, chocolate, etc., would bring on attacks but few have been so fortunate as the authors mentioned in affording relief. To most of us the evidence that allergens are the cause of migraine has still a long way to go to be convincing.

Certain endocrinologists claim that migraine may be due to dysfunction of the pituitary gland. As yet no one can deny this, but the type of evidence put forth to support the argument is somewhat bewildering to the ordinary mind. The ophthalmologists lead us to believe that migraine is often due to eyestrain. I wish it were, and I wish that the type of oculist could be raised up who would correct the offending error of refraction. So far he has eluded me. Or it may be it is associated with disturbance of the genital glands. Its appearance at puberty, its exacerbations about the menstrual period and frequent disappearance at the menopause, and its similarly frequent disappearance during pregnancy are very suggestive. Just what one would do about male patients on this basis raises a difficulty. The statement that migraine is due to some disturbance of the vegetative nervous system is a sort of revelation of the obvious. The almost constant association of sympathetic phenomena with all cases and their predominance in some is well known.

The headache and vomiting remind one of a temporary cerebral tumor and the occasional hemianopia and other visual aberrations suggest a local swelling of the occipital cortex and regions more anterior. All of these symptoms would indicate some process causing temporary swelling of regions of the cortex, but whether of vascular or lymphatic origin no one may yet say. In this connection a verbal communication of Dr. Wilder Penfield's is of interest. He would postulate as a cause of migraine a stimulus arising from some so far unknown cause in the substance of the brain, and transmitted along the sympathetic fibres now known to accompany the cerebral vessels, to the cerebrospinal nerves supplying the head and neck, in the same manner as the pain due to coronary disease is trans-

mitted to the precordium and the arm. Penfield points out that while pressure upon or distention of the dura in other areas is painless, pressure upon the tentorium even with the tip of a hemostat is immediately painful, and the pain is referred to the back of the eye upon the same side; the occipital cortex, from its proximity, is the cerebral region most likely to be affected by such pressure and it is here that visual symptoms would originate.

I would like to quote a statement of Edwin Bramwell's which appears best to summarize the view of the cause of the migraine syndrome.

"In the migraine patient there is some underlying mechanism associated if not identical with the vasomotor system. Development of symptoms may be due to a great variety of accessory causes—toxemia, eyestrain, protein sensitization, psychological repressions. Many seek to establish one of the accessory causes as the essential feature. All claims of the universal efficacy of one line of treatment are mistaken but all may be effective in some cases by removing accessory causes of the disorder. The conception of migraine as due to some innate peculiarity, liable to be excited or aggravated by accessory causes seems the most useful theory."

Upon this view we must base our therapy until a new light dawns.

Being then approached by a patient with symptoms which suggest migraine one cannot dispose of the matter with a wave of the hand and a laxative and a headache powder. The history should be most searching and should attempt to establish or exclude (1) a periodical character to the attack; (2) as accurately as possible the age at onset; (3) the march of the attack should be followed with the presence or not of accessory symptoms as hemianopia, aphasia or ocular manifestations, flashes, spectra or scotomata or accompanying vasomotor features as unilateral flushing, sweating or pulsation of the temporal artery and finally a period of complete freedom between attacks; (4) the onset of the attack following periods of fatigue, especially journeys; or other forms of mental strain; (5) The family history should be searched for evidences of periodical headaches under many disguises.

Nothing less than a complete physical examination should be carried out, with the necessary x-ray examinations and blood and urine examinations for the exclusion of organic disease. In all cases the examination of the ocular fundi is important.

A rigorous examination for errors of refraction is essential.

The estimation of the sugar tolerance is very desirable as is the estimation of the basal metabolic rate.

Protein sensitization tests are of certain usefulness though the rougher method of trial and error with suspicious foods may give equally valuable information. Vaughan and others lay stress upon the attention to not only early reactions but late ones, from six to twenty-four hours after injection.

Lastly the mental examination cannot be ignored and I recall several instances in which the cessation of a mental conflict brought great relief.

Treatment, at present, must be based largely on common sense, with, perhaps, a certain amount of judicious experimentation. It is well known that city dwellers suffer much less from migraine when on a holiday in the country, and the farther from civilization they go, the more free they are from attacks; and following this lead a simplification of life, and as much of it as possible spent outdoors, should be a corner stone of any attempt at therapy. On account of the association of attacks with the menstrual period, it has been suggested that bringing about the cessation of menstruation would be a justifiable therapeutic measure, but in one woman under my care who was a sufferer from migraine and who also had a tuberculous salpingitis, for which total ablation of the pelvic organs was done, the syndrome of the menopause which followed was accompanied by a severer form of migraine than she had before endured.

Elliott and Hurst make a very strong case for accurate correction of errors of refraction and for the necessity of the patient constantly wearing the correcting glasses, though one cynic observes that "He is a fortunate oculist who last examines the eyes after the patient has turned forty-five."

Vaughan and Balyeat are optimistic about their results in treating patients with migraine by diets based upon their reactions to protein sensitization tests. On this line Ball treated twenty cases by intravenous injections of 5 m. of 5 per cent peptone solution as a desensitizing agent and had ten failures and seven cases which were definitely relieved.

T. R. Brown in a study of 110 cases of migraine did sugar tolerance tests upon eighteen cases and in nine found a diminished sugar tolerance and in these, the use of a low starch and sugar-free diet gave great symptomatic relief. The employment of a ketogenic diet after the method employed in epilepsy has been tried, but in my experience with very indifferent results.

There are few drugs in the pharmacopoeia which have not been employed. In my hands luminal given systematically over a long period has in some cases diminished the frequency and severity of the attacks. James Stewart's prescription for the attack was a cup of black coffee and a bed in a cool dark room. In a few instances the ordinary coal tar analgesics have given relief to the headache but more often they have not. In rare cases a hypodermic of morphia has been necessary, but the distressing nausea following it has discouraged its use even

if the danger of habit had not stayed one's hand.

Of late, on the ground that many of the symptoms of migraine are propagated through the sympathetic nervous system the employment of ergotamin has been advocated. Pharmacologically ergotamin is an inhibitor of the peripheral fibres of the sympathetic and is given either by mouth or intramuscularly in the form of ergotamin tartrate or "Gynergen" in doses of one milligram or more. My own experience with it has been most satisfactory in a few cases, but it apparently has no curative effect and only produces cessation of the symptoms, but even this may almost make a Hell into Heaven.

Finally, in these cases in which life has become a burden, relief by surgery may be sought. Dandy reports two cases in which complete relief of hemicrania was brought about by excision of the inferior cervical and first thoracic ganglion of the sympathetic on one side, and in one of the cases no relief had come from a previous excision of the superior cervical ganglion. Penfield has modified this operation by cutting the inner fibres of the fifth nerve which go to the superior division just after they leave the gasserian ganglion and in this way also has given practically complete relief. One realizes, of course, that none of these methods have solved the problem of migraine any more than similar procedures have solved the problem of anginal pain: but anything which can even take the edge off this curse of humanity is a long step in the right direction.

SYSTOLIC GALLOP RHYTHM: A CLINICAL STUDY*

BY WILLIAM P. THOMPSON, M.D.,† AND SAMUEL A. LEVINE, M.D.†

IT is our purpose to present here the results of a clinical study of a group of thirty-five patients with systolic gallop rhythm of the heart sounds seen in the private practice of one of us and to review the literature on the subject. This form of gallop rhythm has received little attention, particularly in the English language, and no comprehensive analysis of any considerable series of patients has been made. It is, in fact, unknown to many clinicians. Much has been written concerning gallop rhythm, but emphasis has been directed almost entirely to the so-called diastolic gallops (protodiastolic, mesodiastolic and presystolic). In general it has been known that such peculiar sounds not only indicate organic heart disease but also connote a rather grave myocardial condition. The subject of this study has such a different clinical significance and can be so easily confused with the former phenomena that it seems appropriate to analyze this aspect of gallop rhythm and to contrast any differences between the two that may exist. At the outset it must be recalled that gallop rhythm is an auscultatory finding on examination of the heart in which three distinct sounds are heard and in which the third or extra sound is appreciably separated from the two normal heart sounds. Diastolic gallops are those in which the abnormal sound occurs somewhere between the second and the first heart sounds and systolic gallops, to which this study is confined, are those in which it occurs between the first and second sounds.

REVIEW OF THE LITERATURE

Description of the Sound: The first description of systolic gallop rhythm was published in 1887 by Cuffer and Barbillion[1]. These authors reported six cases in which the extra sound, much like the first in quality but somewhat shorter in duration, was situated in the "little silence" slightly closer to the normal first sound than to the second. The first sound was normal and associated with the usual systolic pulsation at the apex of the heart. The extra sound appeared after a brief interval following the termination of the first and was also accompanied by an elevation of the precordium just above and inside the apex, at which point the extra sound presented its maximum intensity. The pulsations thus gave a see-saw character to the movements of the chest wall. The gallop sound was not influenced by respiration or by the position of the patient, although it would come and go without apparent cause over periods of hours or days at a time. The authors clearly pointed out that in various patients all intermediaries between a simple prolongation of the first sound and a well-defined extra sound may be encountered, the term gallop being reserved by them for such instances as those in which the extra sound was well defined and significantly separated from the normal heart sounds.

Subsequent descriptions vary somewhat from that of the original authors. Potain[2] and Wolferth and Margolies[3] found the maximum intensity at the base of the heart. Wiedemann[4] found it over all portions of the precordium and over the carotid arteries. He described it as closer to the second sound than to the first and noted its association with a short systolic thrill at the apex and in the fourth and fifth spaces near the sternum. Obrastzow[5] spoke of it as a doubling of the first sound, implying thereby that it was closer to the first than to the second sound. Giroux[6] differentiated the dull muscular quality of the first sound from the higher pitch, drier timbre and valvular quality of the extra sound.

Clinical Features of the Patients Exhibiting

*From the Medical Clinic of the Peter Bent Brigham Hospital.
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Systolic Gallop Sounds: There is little agreement in the literature as to the type of patient in whom one is likely to encounter systolic gallop rhythm, doubtless because of the small number of patients upon which each author based his report. Four of the six cases of Cuffer and Barbillion[1] had typhoid fever, one tuberculosis of the lungs, peritoneum and genital organs, and the sixth kyphosis due to Pott's disease. None of their patients had either heart or renal disease such as are frequently exhibited in diastolic gallop rhythm. Potain[2] found systolic gallop associated with arteriosclerosis of the aorta with atheromata, in typhoid fever and in grippe of the typhoid form. Wiedemann's[4] case had pulmonary tuberculosis. Giroux[6] described systolic gallop rhythm in hypertension with left ventricular hypertrophy. The patients of Amblard[7] had weakened hearts and low blood pressure as part of the general debility of such diseases as typhoid and diphtheria. One of White's[8] four cases was diagnosed as irritable heart. The other three had enlarged hearts, one with auricular fibrillation and another with auricular fibrillation and intraventricular heart block. Wolferth and Margolies[3] found this form of gallop rhythm in two patients, a girl of fourteen years extremely ill with miliary tuberculosis and a fifty-year-old woman with hypertension, coronary arteriosclerosis and heart failure. Thus it appears from the literature that systolic gallop rhythm is encountered in the following three conditions: in the normal heart weakened by a severe general infection, in arterial hypertension and in the presence of atheromatous change in the aorta. No mention was made as to its benignity or its occurrence in otherwise healthy individuals.

Autopsied Cases: Autopsies are reported in the literature in but four instances. The heart of one of the cases of Cuffer and Barbillion[1] was contracted and normal, the patient having died of typhoid fever with intestinal hemorrhage. Another presented a dilated and flaccid heart that was otherwise normal, this patient having died of tuberculosis. Both of Obrastzow's[5] patients had atheromatous change in the ascending portion of the aorta, one with dilatation. The heart itself was not otherwise mentioned. From the meagre autopsy data we know only that systolic gallop rhythm may occur without objective organic disease of the heart. Gallavardin[9] reported autopsies on three patients with metallic clicking sounds occurring in systole. All three had strands of pleuropericardial adhesions to which Gallavardin attributed the sounds. Likewise, Lian and Deparis[10] reported fifty cases with clicking sounds during systole and referred to the possible association of this finding with pleuropericardial adhesions, although no postmortem studies were made.

Mechanism of Production: As to the mechanism by which systolic gallop rhythm is produced, the literature offers only reasoning by inference. Cuffer and Barbillion[1] thought that the first sound and the gallop sound were produced by the two parts of a double systolic effort made by a ventricular myocardium so weakened that a single effort was incapable of raising intraventricular pressure to a degree sufficient to open the semilunar valves. They felt that one would be likely, then, to encounter the gallop sound in all states in which the heart gives way in consequence of myocardial weakness of any cause, whether such weakness be primary or the result of a general affection of the body. They believed the double systolic elevation of the precordium and the plateau observed in the upstroke of the apex cardiogram to be in keeping with this idea.

Potain[2] gave origin to the concept of arterial production of the extra sound. According to him, an aorta diseased by atheromatous change or by general weakening of its wall in such diseases as typhoid may produce a sound when stretched to the limit of its distensibility by the inflow of blood from the left ventricle. Under normal conditions, he felt, the aorta is never stretched to its limits and a sound is not produced. Wiedemann[4] adopted the arterial production theory by the exclusion of other factors and on the basis of evidence of sclerosis of the radial arteries.

Obrastzow[5] reasoned that there was an increase in the period of isometric contraction of the ventricle, the first sound being produced by the closure of the auriculoventricular valves and the extra sound by the opening of the semilunar valves and the commencement of ejection of blood from the ventricle, these two elements being fused into one sound in the normal heart. Thus the condition of the myocardium and the presence of arterial hypertension must play no unimportant rôle. Bard[11] later concurred in this idea. Giroux[6], whose patients had hypertension and left ventricular hypertrophy, agreed to the theory of a lengthened presphygmic period and to the dissociation of the muscular and valvular elements of the first sound, but thought that the extra sound would not appear unless the valves were sclerosed.

Amblard[7] studied the blood pressure in his patients with typhoid or diphtheria and systolic gallop rhythm or a tendency to it. He found that on slight exercise the systolic and diastolic blood pressures rose from their previously abnormally low levels to approximately normal levels, at which time the gallop sound appeared. If exercise were carried still farther, the pressure, particularly the systolic, fell markedly, whereupon the sound disappeared. He concluded that after slight exercise his patients were suffering from a relative hypertension which produced the sound in the presence

Case No.	Age Years	Sex	Chief Complaint
1	28	F	Told she had heart diseas
2	19	F	Irregular rhythm had bee
3	21	M	Murmurs had been heard. pitation when nervous.
4	71	M	Pain on exertion 8 years attack 1 month ago.
5	43	M	Tired. Losing weight.
6	11	F	Murmur had been heard joint pains.
7	37	F	Nausea.
8	42	M	Nervous since seeing a r Pains in left chest.
9	46	F	Weak.
10	61	M	Tired. Occasional dull ach heart.
11	64	M	Dyspnea. Precordial oppr
12	38	M	Tired. Ache about heart.
13	28	F	Tired.
14	40	M	Wanted examination.
15	32	M	Tired. Sighing respiratio
16	50	M	Constriction lower sternun ertion.
17	22	F	Sternal pain. Fainting Heart consciousness.
18	23	F	Palpitation and pain in hea told she had a murmur.
19	35	F	Nervous. Exhausted.
20	59	F	Cough following pneumon
21	44	M	Slight palpitation.
22	31	F	Tired. Pain about heart.
23	34	M	Nausea. Wanted heart ex
24	18	M	Something queer had bee in heart.
25	43	M	"Staggering" sensation risi chest to neck.
26	25	F	Aerophagia. Belching of
27	28	F	Tired. Mild joint pains. dial pain once.
28	44	M	Epigastric pain after meals thing queer found in hear
29	57	M	Severe precordial pain ago.
30	37	M	Ache about apex.
31	65	F	Slight pain at apex.
32	56	F	Nervous. Palpitation.
33	49	M	Sternal pain.
34	25	F	Ache over apex. Tired. tion.
35	60	M	Tired. Slight pain at apex

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TABLE 1

Complaint	Heart Rate Beats per Minute	Blood Pressure	Electrocardiogram*	Clinical Diag
art disease.	90	116/64	Normal.	Pregnancy.
n had been found.	94	110/80	A-V nodal rhythm.	Functional heart dise
en heard. Sl. pal- ervous.	140	160/96	Normal.	Hypertension.
n 8 years. Heart ago.	81	130/66	$T_{2,3}$ negative. Not coronary type.	Angina pectoris. Co bosis. Diabetes mellit
veight.	—	134/78	Normal.	Incipient tuberculosis
een heard. Mild	90	105/60	———	Mild rheumatic state.
	86	110/70	Normal.	Secondary anemia. Gastric neurosis.
eeing a man die. st.	80	114/70	Very slight L. A. D.	Normal heart.
	98	178/108	Normal.	Hypertension.
al dull ache about	65 to 79	156/98	Normal.	Slight hypertension.
rdial oppression.	—	125/75	Normal.	Coronary sclerosis.
ut heart.	84	132/86	Normal.	No disease.
	108	122/70	———	No disease.
tion.	88	124/70	Normal.	No disease.
respiration.	80	120/85	Normal.	Neurasthenia.
er sternum on ex-	70	152/96	$T_{2,3}$. Coronary type.	Angina pectoris. Hypertension.
Fainting spells. ess.	—	128/90	———	Irritable heart.
ain in heart since urmur.	65	120/70	Normal.	No disease.
sted.	93 to 105	142/90	Normal.	Nervous fatigue.
pneumonia.	88 to 100	170/95	Normal.	Hypertension.
n.	90	160/80	Slight L. A. D.	Slight hypertension.
ut heart.	82	125/70	Marked L. A. D.	Benign systolic murmu
l heart examined.	63	110/70	Normal.	Normal heart.
had been heard	70	142/85	Normal.	Sinus irregularity.
sation rising from	84	108/75	Normal.	No disease.
ching of gas.	90	130/70	L. A. D.	Habit spasm.
nt pains. Precor-	—	—	———	Smouldering rheumatic
fter meals. Some- d in heart.	92	112/70	Normal.	Peptic ulcer.
al pain 1 week	62 to 70	112/70	Marked L. A. D. Coronary $T_{2,3}$.	Coronary thrombosis.
.	65	—	Normal.	Normal heart.
pex.	—	180/125	———	Hypertension.
ation.	65	126/80	Occasional V. P. C.	Benign cardiac irregul
	74 to 92	150/85	Coronary $T_{2,3}$.	Angina pectoris. Calcification of pericar
Tired. Palpita-	88 to 111	118/75	Occasional V. P. C.	Benign cardiac irregul
in at apex.	74	112/75	Left bundle branch block.	Bundle branch block.

Cases 4 and 16 were the only ones with cardiac hypertrophy

*L. A. D. = Left axis deviation.
V. P. C. = Ventricular premature contraction.

TABLE 1

lood ssure	Electrocardiogram*	Clinical Diagnosis	Systolic Gallop Rhythm
6/64	Normal.	Pregnancy.	Marked about apex in both positions.
0/80	A-V nodal rhythm.	Functional heart disease.	Base only. Almost gone 13 months later.
0/96	Normal.	Hypertension.	Apex only.
0/66	$T_{2,3}$ negative. Not coronary type.	Angina pectoris. Coronary thrombosis. Diabetes mellitus.	Loudest of the 3 sounds.
4/78	Normal.	Incipient tuberculosis of lungs.	Apex only, when recumbent only.
5/60	———	Mild rheumatic state.	Systolic murmur first examination. No murmur, but gallop 13 months later.
0/70	Normal.	Secondary anemia. Gastric neurosis.	Marked at apex only in both positions.
4/70	Very slight L. A. D.	Normal heart.	Apex only. Better in recumbent position.
8/108	Normal.	Hypertension.	Slight intensity.
6/98	Normal.	Slight hypertension.	Apex only. Better while flat.
5/75	Normal.	Coronary sclerosis.	Moderate intensity.
2/86	Normal.	No disease.	Typical.
2/70	———	No disease.	Apex only.
4/70	Normal.	No disease.	Typical.
0/85	Normal.	Neurasthenia.	Apex only.
2/96	$T_{2,3}$. Coronary type.	Angina pectoris. Hypertension.	Moderate apex only. Louder in sitting position.
8/90	———	Irritable heart.	Moderate intensity.
0/70	Normal.	No disease.	Apex only.
2/90	Normal.	Nervous fatigue.	Apex only.
0/95	Normal.	Hypertension.	Marked. Louder recumbent. Three years later louder sitting. Present 12 of 13 examinations in 7 years.
0/80	Slight L. A. D.	Slight hypertension.	Marked.
5/70	Marked L. A. D.	Benign systolic murmur.	Typical.
0/70	Normal.	Normal heart.	Apex only. Both positions.
2/85	Normal.	Sinus irregularity.	Typical.
8/75	Normal.	No disease.	Apex only while recumbent.
0/70	L. A. D.	Habit spasm.	Typical.
—	———	Smouldering rheumatic state.	Very loud in all positions.
2/70	Normal.	Peptic ulcer.	Recumbent only.
2/70	Marked L. A. D. Coronary $T_{2,3}$.	Coronary thrombosis.	First examination only. Not in 5 examinations next 2 years.
—	Normal.	Normal heart.	Typical.
0/125	———	Hypertension.	Slight intensity.
6/80	Occasional V. P. C.	Benign cardiac irregularity.	Apex only.
0/85	Coronary $T_{2,3}$.	Angina pectoris. Calcification of pericardium.	Present 4 of 7 examinations in 8 years. Loud whole precordium, best at apex. Diminished in sitting position.
8/75	Occasional V. P. C.	Benign cardiac irregularity.	Absent once. Present 5 years later.
2/75	Left bundle branch block.	Bundle branch block.	Apex only.

s 4 and 16 were the only ones with cardiac hypertrophy.

*L. A. D. = Left axis deviation.
V. P. C. = Ventricular premature contraction.

of a weakened myocardium. White[12] has stated that the cause is unknown, but that it may possibly be deformity of valves, chordae tendineae, pericardium or pleura.

Opinion as to mechanism is, then, roughly divided into two basic ideas, that of a lengthened period of isometric contraction of the ventricle with resultant dissociation of the elements of the normal first sound and that of production by a diseased or weakened aortic wall.

Prognostic Significance of Systolic Gallop Rhythm: There is no intimation in the literature that systolic gallop rhythm bears the ominous prognostic significance so well known in diastolic gallop rhythm. The cases are too few, however, to be of any statistical value. Several of the reported cases died of frankly non-cardiac causes. It is possible that this form of gallop rhythm in the presence of general infection implies a severe general debility, but whether such debility is more severe than in those patients who do not exhibit systolic gallop sounds we do not know. Likewise, in those patients with organic heart disease or arterial hypertension we cannot say that the prognosis is worse with than without systolic gallop rhythm. Several cases of recovery from infections, with disappearance of the sound, are reported. Some authors, notably White[12], Wolferth and Margolies[3], and Macleod, Wilson and Barker[13] have regarded it as without significance.

THE PRESENT SERIES

We have observed the gallop sound placed in the systolic phase of the heart cycle in thirty-five patients over a period of eleven years. (See table 1.) The relative frequency of this type of gallop rhythm is reflected by the fact that during the same period 186 patients with diastolic gallop rhythm were observed. Approximately 16 per cent, then, of patients showing gallop sounds that have come under our observation have exhibited the systolic variety.

Quality of the Sound: In all of this group the extra sound was separated from the normal first and second sounds by an interval sufficiently long so that we clearly felt we were dealing with an additional rather than a split sound. In general the extra sound resembled in quality the normal first sound. Variations in quality were encountered, at times the accessory sound having somewhat more of a valvular quality resembling the second sound. It is possible that some of these may be similar to the metallic clicking sounds supposedly due to pleuropericardial adhesions.

Intensity of the Sound: The intensity of the extra sound was variable from patient to patient and in the same patient on different examinations. In twelve cases we have made clear notes in this connection. In two it was of slight intensity, that is, just loud enough to be positively identified as a distinct extra sound, in four it was of moderate intensity and in six it was as loud as or louder than the other heart sounds. In the majority of our series it was heard only at the apex of the heart or with maximum intensity at the apex. In but a single case was it heard only at the base.

Effect of Position: The position assumed by the patient during the examination had considerable influence on the intensity or even the presence of the sound. Our notes specifically mention this relationship in twelve instances. In three cases the sound was heard only while the patient was recumbent, disappearing when the sitting posture was assumed. In four cases it was heard in both positions, the intensity being greater in the recumbent in three and in the sitting position in one. In four cases it manifested an equal intensity in both positions. In another it was of marked intensity while the patient was supine and practically absent when he sat up. Three years later this relationship was reversed.

Effect of Rate: In this series of cases gallop rhythm was heard with varying rates of the heart beat. There were ten instances in which it was present while the rate was under 80 and five when it was under 70. In the others the rate was higher, occasionally reaching levels over 120. This is unlike the relationship between heart rate and diastolic gallops, for it is very rare to find these gallops present when the heart rate is slow, especially under 70.

Constancy of the Sound: The constancy with which the sound was observed in a patient who had once exhibited it was also variable. In three cases it was noted after its absence on a previous examination. One of these had a mild rheumatic infection and a systolic murmur; thirteen months later the murmur had disappeared and systolic gallop rhythm was present. In one case the sound had practically disappeared when the patient was examined one year later. In one the sound was observed on twelve of thirteen examinations over a period of seven years, while another exhibited it on four of seven examinations over eight years. One had the sound when seen one week after an acute coronary closure. He made a good recovery and it was not heard again on the five examinations during the next two years. Adequate follow-up data on this group over a long period are not available since the patients were largely seen in consultation and remained under the immediate care of their own physicians.

Clinical Features of the Group: By and large the patients in this series made up a rather miscellaneous group. There were some with mild and others with severe cardiovascular disease. There were still others who had organic disease not involving the cardiovascular system and finally a group which had no organic disease whatever, merely manifesting

minor functional disturbances. There were no patients in the group who had severe acute infections such as typhoid fever or diphtheria similar to those reported in the literature. This is perhaps due to the fact that such acute infections are rarely encountered in the practice from which these cases are drawn. Only two patients in the group had known infections of any sort, both having mild rheumatic fever. Eighteen patients or half the group had no demonstrable organic disease whatsoever and twenty-three or two-thirds had no detectable cardiovascular disease.

The presenting complaints of most of these patients were strikingly either mild or bizarre. Seven were sent by their own physicians because something queer had been heard on auscultation. Two came voluntarily because they wanted their hearts examined. Only one of these nine patients had a notable symptom, a woman whose palpitation and pain about the heart had been annoying since she was told that she had a heart murmur. Eleven complained of being tired or lacking vitality. One man stated that he was nervous since witnessing a death. Sixteen patients complained of pain about the apex of the heart, but only five were regarded as having coronary artery disease. In the others the pain was mild, vague and precipitated by nervousness and not by exertion. Belching of gas, nervousness, palpitation and peculiar sensations in various parts of the body were common complaints. Actual physical incapacitation was entirely absent except to a slight degree in the five patients who had coronary artery disease. The striking thing about the group was that the majority were "nervous" people who were concerned about the possible existence of heart disease.

Of the twelve patients who did have cardiovascular disease, five had disease of the coronary arteries, in three of whom occlusion had occurred. Two of these five and six others had arterial hypertension. The degree of hypertension was not marked, however, as only three had systolic tensions of over 160 mm. and only two had diastolic tensions of over 100 mm. The other patient in the group with cardiovascular disease was a man of sixty years who had left bundle branch block without other evidence of heart disease. There were none with valve defects. It is notable that in the entire series there were only two patients whose hearts were clinically enlarged. Equally notable is the fact that in not a single instance was there subjective or objective evidence of congestive heart failure.

Electrocardiograms were obtained in thirty of the group. Significant abnormalities, without consideration of left axis deviation or occasional premature contractions, occurred in only five patients. Four of these had coronary disease and one had bundle branch block. Auriculoventricular nodal rhythm occurred in one of the group without heart disease, but this we have not considered a significant abnormality.

Age: There is a fairly sharp division of the groups with and without cardiovascular disease according to age. Among those with cardiovascular disease there was but one less than forty-four years old, a man of twenty-one with slight arterial hypertension, while in the group without cardiovascular disease there was but one who was more than forty-four years of age. Thus almost without exception the older patients in our series had cardiovascular disease while the younger ones did not. The extremes of age in the entire series were eleven and seventy-one years.

Sex: The sexes were represented by nineteen males and sixteen females. Among those with cardiovascular disease, however, there were twice as many males as females while the sexes were equally represented in the group without cardiovascular disease.

Prognosis: The prognostic significance of systolic gallop rhythm is suggested by the fact that none of the group are dead, and most are in a good or excellent state of health. This is in striking contrast to the fact that 46 per cent of the cases with diastolic gallop observed during the same period of time are known to be dead, the remainder being unheard from or known to be in poor condition. The dead who showed a diastolic gallop rhythm lived an average of ten months and twenty days after the detection of the gallop; the living have so far survived an average of about fifteen months. The patients with systolic gallop rhythm have already lived an average of more than five years and for the most part are well.

The absence of symptoms of myocardial insufficiency of any appreciable extent in those with heart disease, the slight degree of arterial hypertension in those who exhibited it, the rarity of cardiac enlargement and the complete absence of all signs of congestive failure make it appear that this variety of gallop rhythm has no unfavorable influence upon the subsequent course of the patient's life.

The importance of systolic gallop rhythm lies in the fact that it may be confused with diastolic gallop and an incorrect prognosis given as a result of this error. In a few cases we have experienced difficulty in timing the extra sound. The following procedure, however, has been useful in deciding that the abnormal sound occurred between the first and second sounds rather than between the second and first. During auscultation the stethoscope is first placed at the apex and then rhythmically moved with each heart beat to points nearer and nearer to the aortic area. It will generally be found that the sound that gradually disappears is the

middle one of the three and the examiner is therefore left with the normal two heart sounds on reaching the base of the heart. We are fully aware that indisputable evidence that the gallop sound was truly systolic could only have been obtained with sound tracings photographed simultaneously with other events of the cardiac cycle such as those recorded in the electrocardiogram. The sharp clinical distinction and subsequent course of the cases included in this study as contrasted to those with diastolic gallops are fairly satisfactory proof that the bedside findings and terminology were valid.

Mechanism of Production: As to the mechanism by which systolic gallop rhythm is produced we have nothing to offer from our series except in so far as the previously mentioned theories may be applied here. We cannot speak of atheromatous plaques in the ascending portion of the aorta without autopsy material. It does not appear, however, that such degenerative changes could be an important factor in our cases with such a preponderance in the younger age group. It is true that many of our patients were asthenic individuals. This would be consistent with Potain's theory of production of the sound by distention of an aortic wall the tone of which is diminished. Certainly the physical state of our patients, however, is not comparable to that which obtains in typhoid fever. This can scarcely explain all instances. The other theories also seem inadequate, although pericardial or pleuropericardial adhesions may possibly account for some of these cases.

SUMMARY

Thirty-five patients with systolic gallop rhythm observed over a period of eleven years are reported. This number represents 16 per cent of all patients with gallop rhythm encountered during this period.

The extra sound in systolic gallop rhythm is placed in systole between the normal first and second sounds. In most cases it has a quality resembling the normal first sound. Its maximum intensity is usually in the region of the apex of the heart. Its intensity is variable in different patients and occasionally in the same patient from time to time. It may alter its intensity or even disappear with change in the position assumed by the patient, although generally it is loudest in the recumbent position. It may also appear or disappear without apparent cause.

Two-thirds of the group had no cardiovascular disease. Most of them had no complaints, having been seen in consultation because of suspected heart disease, or they presented bizarre complaints of a minor or functional nature. Most of them were "nervous" people. The remainder of the group, twelve in number, had demonstrable cardiovascular disease. Five of them had coronary artery disease, two of these and six others had arterial hypertension, usually mild in degree, and one had bundle branch block without other evidence of cardiovascular disease. Valve defects, congestive failure or congestive signs of any sort were not found. Only two patients had cardiac enlargement. Significant electrocardiographic abnormalities were absent except in four of those with coronary disease and the one with bundle branch block. No real incapacitation was present except in those with coronary artery disease.

Extremes of age were eleven and seventy-one years. With one exception in each group, those below forty-four years of age had no cardiovascular disease, those above forty-four had such disease. Males were predominant in the group with cardiovascular disease, while there was no difference in the number of males and females in those without it.

None of the group are dead at the time of this report, while 46 per cent of the group with diastolic gallop observed over the same period are dead. The rarity of cardiac enlargement and physical incapacitation, the slight degree of arterial hypertension in those who had it and the complete absence of congestive signs all point to the benignity of systolic gallop rhythm.

It appears that none of the proposed theories as to causation of the extra sound can satisfactorily account for all cases.

CONCLUSIONS

1. Systolic gallop rhythm is more frequent than is commonly supposed.
2. It occurred in this series predominantly in "nervous" people. Heart disease is more often absent than present in patients with systolic gallop rhythm although serious heart disease may be present.
3. It has no unfavorable influence on prognosis.

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THEELIN THERAPY IN VULVOVAGINITIS

BY RICHARD BETTS PHILLIPS, M.D.†

SINCE the introduction by Lewis[1] of theelin, the estrogenic hormone, in the treatment of vulvovaginitis in 1933, there have been a number of papers published on this particular aspect of hormone therapy: J. Brown[2], Huberman and Israeloff[3], Miller[4], and in England, Nabarro and Signy[5]. Other very interesting work has been published recently on the chemistry of this hormone, its apparent relationship to carcinogenic tar derivatives, and its effect on the male and female organism; Leo Loeb[6], Cook, Dodds, and Hewett[7], Burrows and Kennaway[8], and A. Lacassagne[9]. (Vide infra.)

Theelin* is the name given to the estrogenic substance by Parke Davis. Schering prepares it as Progynon. G. W. Carnrick has named its preparation Thelestrin; Squibb calls it Amniotin; and still other names by which this hormone is known are Menformon, Estrin, and Folliculin. Theelin has been found to have the formula $C_{18}H_{22}O_2$. It is lipoidal in type, with absence of nitrogen, and possesses a structural picture very similar to the male sex hormone, the corpus luteum hormone, and cholesterol, all of which are phenolic compounds.

The hormone theelin may be administered either intramuscularly or orally. The oral preparation is called Theelol by Parke Davis, and the oral dosage is approximately five times greater than the intramuscular. Dosage is estimated in rat units or in international units. The rat unit is approximately 3.3 times stronger than the international unit. The international unit is defined as the activity of one ten-thousandth of a milligram of a standard international crystalline powder identical with the theelin first described by Dr. Doisy. There are about 3,000 rat units per milligram of theelin. One Doisy or rat unit is equivalent to 3.3 international units. A Doisy rat unit is the smallest amount of estrogenic hormone which will induce estrus in mature but ovariectomized rats, as judged by cornification of epithelial cells in vaginal smears. The hormone must be the smallest amount which will cause this effect when administered in three divided doses, four hours apart. Twenty rats must be used in each test, and 75 per cent of these animals must show a typical response. One rat unit is equivalent to five mouse units. Wide variations in dosage have been described, from 25 rat units as administered by Raglan Miller[4] intramuscularly in patients in whom a theelin reaction has been established, to 50,000 international units administered orally and intramuscularly in one dose by Nabarro and Signy[5] of London.

*One-half of the Theelin used was kindly presented to us by Parke Davis & Company.

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Edgar Allen[10] in 1928 showed that in the Macaca rhesus monkey a proliferation and thickening of the vaginal epithelium follow shortly after the administration of the ovarian hormone. Herein lies the rationale of this treatment as applied to vulvovaginitis. That is to say, one hopes that, by creating a temporary transformation of the immature vaginal epithelium as seen in young girls into one which is thickened and adult in type, a cure may be established. The upper layers of the vaginal epithelium become cornified, and increase in thickness from five to thirty layers or more. There is pronounced sloughing of this outer or functionalis layer (see figures 1 and 2). Furthermore, there is a tremendous activity demonstrable in the basal cell layer, with mitotic figures in the cell nuclei and a heaping up of what might be called swollen cells in the intraepithelial layer or the zone midway between the functionalis and basalis layers (see figure 2). It is thought that the sloughing of the epithelial cells (see figure 3) takes with them gonococci which are embedded in the uppermost layers of the epithelium. Furthermore, by keeping up the reaction over a moderate length of time (several months), one hopes to create a more resistant vaginal wall and thereby to prevent reinfection or relapse.

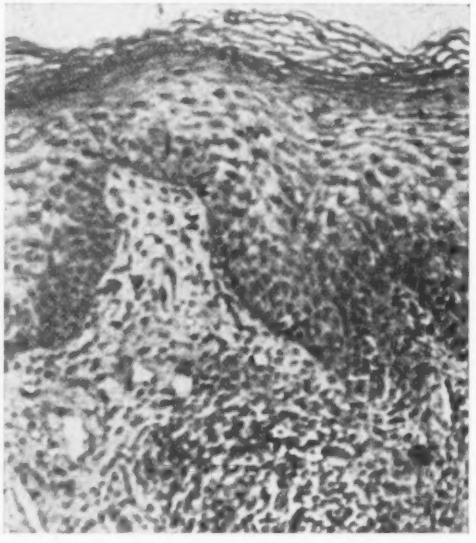

FIG. 1. S. B., aged 8.
Vaginal epithelium removed November 15, 1934. Treatment begun October 11. Total number of rat units of Theelin to November 15, 1450. The epithelium shows cornification, desquamation, and marked hypertrophy. It is of a thickness of approximately thirty layers. The basal cells are undergoing active proliferation. The uppermost layer of the functionalis or outer layer can be seen to be desquamating.

In our series of thirteen cases, treated in the Out-Patient Gynecological Department of the Boston City Hospital, we found eleven of the

children to have positive smears at the beginning of treatment. The other two had suspicious smears, and all had from +++ to ++++ discharges. The smears were loaded with pus

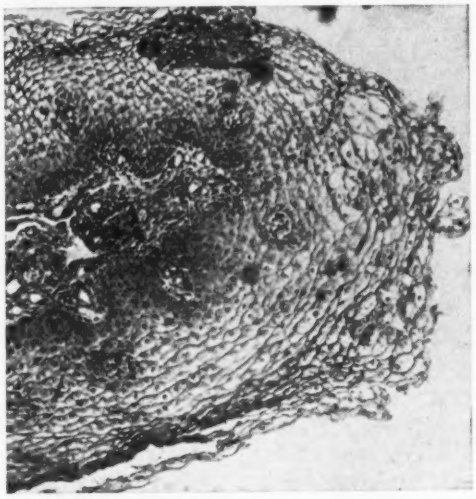

FIG. 2. M. P., aged 6.
Biopsy November 15, 1934, four weeks after treatment had been instituted with Theelin. The patient had received 3300 rat units of Theelin at this time. The smears were negative, although a number had been positive in the preceding month. Notice the cornification, desquamation, and thickening of the epithelium. The basal cell membrane is hyperactive. The arterioles are distended, and the intra-epithelial layer shows what might be called swollen or bulbous cells, while the functionalis layer is seen to be shedding flattened squamous epithelium.

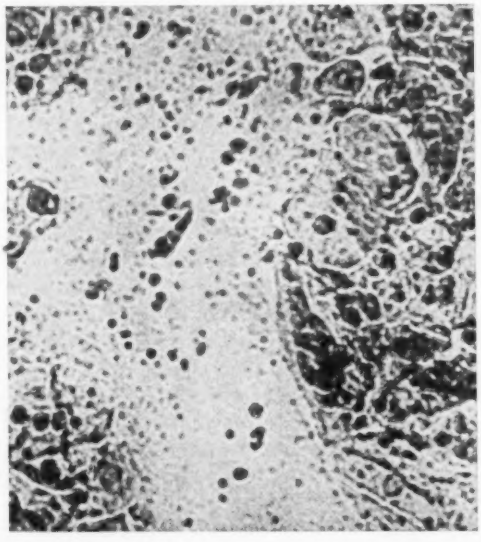

FIG. 3. M. P., aged 6.
Smear taken with platinum loop on November 15, 1934, same day as biopsy (see figure 2), showing large numbers of desquamated epithelial cells which are *cornified*. There are still a few pus cells present, but there were no gonococci evident. Both this patient and her sister, aged three and a half, had positive smears in October.

cells, and gram-negative diplococci, both intracellular and extracellular in large numbers. Six patients had marked inflammatory reddening of the vulva, one with excoriation. Urethritis was present in two. Two children had marked lower abdominal pain with slight temperature. In one of these patients (M. J.), a little colored girl, aged six, typical gram-negative intracellular diplococci were found on performing direct peritoneal aspiration (Dr. J. Tartakoff). This latter case was our only patient who was hospitalized. She had been admitted with a diagnosis of acute appendicitis.

Our plan of treatment was as follows: Each patient received approximately from 700 to 900 rat units, administered in three divided doses weekly. The smallest amount of theelin received by any patient was 2100 rat units, and the largest was 4,460 rat units. Figures 1 and 2 show the effect of the estrogenic hormone on the vaginal epithelium following the administration of 1,450 rat units in the one case, and 3,300 in the other. It would appear that the theelin reaction is established when the patient has received in the neighborhood of 2,000 units. We used the theelin in oil preparation exclusively, not the aqueous solution. The former preparation is supposed to permit of slower and more uniform absorption of the hormone.

Weekly smears were taken throughout the entire period of treatment. The smears were taken by means of introducing a platinum loop into the vagina under reflected light, and scrapings of the vaginal walls obtained. After the first one or two examinations, we found that practically all the patients stood the examination with the greatest of ease. We performed vaginal biopsies once on each patient (see figures 1 and 2). On our charts we recorded the character of the theelin reaction as evidenced by the comparative number of cornified epithelial cells in the microscopic field, a diminishing amount of pus cells, and, of course, the presence of the gonococcus. It was remarkable to note the rapidity with which the smears became loaded with epithelial cells in a short space of time, where previously there had been practically none of these cells. In every case one can notice a marked grayish tumescence of the hymen, visible to the naked eye. This is especially noticeable in colored girls. Raglan Miller[4] describes what he calls the "glassy" appearance of the vaginal smear when it consists almost entirely of epithelial cells, as contrasted with the "opaque" appearance when the smear is taken at the beginning of treatment and consists mostly of pus. We found the knee-chest position to be the best for securing vaginal wall scrapings. Figure 3 shows the large number of epithelial cells of adult type which nearly fill the microscopic field after the reaction is well established. Notice the contrast in these cells and the thin oval immature cell found before treatment.

The average age in our group was six and one-half, the youngest three, and the oldest ten.

The average number of rat units of theelin administered was 3,160.

At the end of ten weeks' treatment, when all patients were regarded as evidencing negative smears and no discharge in ten, and very slight discharge in three, all treatment was discontinued for six weeks. At the end of this time,

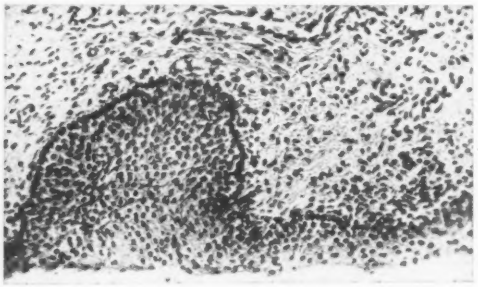

FIG. 4.
Vaginal epithelium of infant two and three-quarter months old. Autopsy specimen. In general but little change in thickness of layers is noted up to about ten years of age. Courtesy of Robert M. Lewis, M.D., Yale University School of Medicine, New Haven, Connecticut.

all were examined again and it was found that 70 per cent (nine out of thirteen) had relapsed. We do not believe that reinfection from extraneous source occurred in any of them. All mothers and fathers had been carefully checked up. Of the nine who were thought to have relapsed, three had positive smears, and six had suspicious smears. All nine had a return of their discharge, but not of such severity as before treatment with theelin. The four who were presumably cured were all subacute cases, and they have remained apparently cured to this date, April 1, 1935.

The economic and social features of vulvovaginitis are serious and far reaching. Oppenheimer and Everett[11] have published an interesting article on this aspect of the disease, and describe forty-three children who were kept out of schools in Washington, D. C., for from one to four years. We ourselves had one patient (A. de C.), aged eight, who was kept out of school for a year and a half and whom we finally were able to have taken back to school only after repeated effort. Oppenheimer and Everett[11] further emphasize the great loss, both economic and sociologic, which this disease may be responsible for.

Theelin is a most potent hormone, and its use is still attended with a certain unknown danger as to what the end result on the patient may be. By its exhibition, menstruation can be caused experimentally in ovariectomized women and monkeys, and endometrium which has been atrophic can be proved to show hyperplasia (Werner and Collier[12]). Lacassagne[9] has demonstrated the fact that the male may be influenced by theelin. He showed that following injection of estrogenic substance into male mice, the posterior lobe showed marked hypertrophy. He also showed that it was possible to increase the mammary cancer rate in mice by increasing the estrogenic substance. Burrows and Kennaway[8] have produced estrus with enlargement of the horns of the uterus in mice and complicated with pyometra and peritonitis merely by applying this hormone to the non-epilated skin of the back. C. Clauberg[13] showed that it is possible to stimulate even the smallest adult human uteri by means of large doses of follicular hormone and proved this by salpingography. Leo Loeb[6] and Lathrop and Loeb[14] demonstrated that with mice in whom early oöphorectomy had been performed, there occurred a very marked diminution in the cancer ratio both in mice possessing a cancer susceptibility and in those that did not. Leo Loeb[6] has further emphasized the apparent close relationship between estrogenic hormones and certain carcinogenic derivatives of tar. Cook, Dodds, and Hewett[7] in 1933 have produced estrus successfully in mice by the use of a synthetic compound which is chemically closely allied to tar. Doisy, Veler, and Thayer[15] showed that one milligram of the crystalline estrogenic hormone is equivalent to 3,000 rat units in potency. On the other hand, Robert T. Frank[16] demonstrated that no estrogenic hormone could be detected one-half hour after injecting 2000 mouse units into a rabbit and that none could be found in the urine or tissues in the succeeding twenty-four hours. However, since it is well known that estrogenic substance will produce active epithelial cell proliferation (see figures 1 and 2), the question which naturally arises is, Will there be any harmful change in these young girls in either the near or the remote future? From a review of the results obtained to date in several clinics, and the experimental work on animals, one can feel moderately certain that the possible damage to any individual is minimal. J. Raglan Miller[4] reported one case recently in which he had the opportunity of performing a biopsy on an ovary of a child who had received 1100 rat units of theelin, and the organ proved to be quite normal. Novak[17] states in a very recent article that estrogenic substance is not a stimulant to ovarian activity, and adds: "The fear that pelvic hyperemia produced by estrogenic substance may predispose to uterine and tubal extension of the vaginal infection is probably more apparent than real." This is in conformity with the progress of one of our cases, M. J. (Vide supra.) Nabarro and Signy[5] in London reported breast hypertrophy in one case which regressed upon cessation of treatment. They report no untoward results in any of their twenty cases, although they gave as much as 10,000 to 50,000 units intramuscularly in one dose, sometimes repeated, and in several cases 1,000 units per day for approximately three months. In three children receiving 3,000 rat units daily, the average length of treatment was cut down to twenty-eight days, and the last

positive smear was found sixteen days after beginning of treatment. Relapse occurred in fourteen out of twenty after having been home an average of two months. These writers advocate large dosage treatment, 4,000 units by mouth at a time. Raglan Miller[4] believes that in new cases treatment should be continued from four to six weeks with smaller doses in the neighborhood of 100 rat units daily, and once the theelin response has been established, then vigorous squamous cell reaction should be maintained for several months. This can be accomplished with a greatly decreased number of rat units, administered weekly. Miller further believes that estrogenic hormone is of value, no matter what organism may be responsible for the vulvovaginitis.

In June 1935 J. Thornwell Witherspoon[18] of Tulane has reported an unsuccessful series of vulvovaginitis cases[10] treated with estrogenic hormone, none of whom were cured. They all showed temporary improvement, however, during the middle of his two to three months' period of treatment. His results therefore have been slightly worse than mine. His dosages were somewhat similar.

CONCLUSIONS

1. Thirteen girls were treated in the Out-Patient Department of the Boston City Hospital with *theelin only* for a period of from four to six months.

2. The patients received approximately the same amount of theelin, the average number of rat units being 3,160. The average age was six and one-half.

3. The discharges cleared up rapidly in all cases to a greater or less degree, and smears became negative in every case within four to six weeks of treatment. Six weeks after cessation of all treatment 70 per cent of the patients (nine out of thirteen) "relapsed". Two of the remaining four patients continued to have slight discharge which was negative, and which cleared up after several more weeks of treatment. Two of the nine were cured after more treatment with theelin. Thus, seven appeared to be in statu quo in the final analysis.

4. No harmful results were noticed in any of our patients. Larger doses than we gave should not be administered, since the epithelial response may be obtained with the doses outlined above. Larger doses *may* cause scar-tissue formation in the ovaries, and it is possible that the menarche in these girls may be delayed or otherwise interfered with. These possibilities will be questioned until a report is published later, dealing with the onset of the catamenia in girls who have been treated with theelin.

5. Theelin (or other estrogenic hormone) may be used in the treatment of vulvovaginitis *in conjunction with* our other and standard methods of treatment. The cost has recently decreased considerably.

6. The *criteria* in following the treatment are:

1. The presence of Gonococci:
   (a) Intracellular,
   (b) Extracellular,
   (c) Absent,
2. Presence of Pus:
   1 plus
   2 plus
   3 plus
   4 plus
3. Epithelial Cells
   (a) Amount
   (b) Type, immature oval, adult cornified,
   (c) Appearance of slide, "glassy", or "opaque",
   (d) Biopsy of vaginal epithelium.
4. Hymen
   Grayish and edematous when the estrogenic hormone reaction is established.

The Vaginal Epithelium Blocks were made by the Tufts Pathology Laboratory.

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CASE RECORDS

of the

MASSACHUSETTS GENERAL HOSPITAL

ANTE MORTEM AND POST MORTEM RECORDS AS USED IN WEEKLY CLINICAL-PATHOLOGIC EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 21471

PRESENTATION OF CASE

First Admission. A thirty-five year old white American janitor was admitted complaining of swelling of the legs.

Two weeks prior to entry the patient developed a sore throat associated with nasal discharge and mild headache. These symptoms continued for about three days and then subsided. At this time he noticed swelling of his ankles and, in the absence of other symptoms, continued with his work. The swelling gradually extended up his legs and he began to fatigue readily. A slight non-productive cough developed. He had a nocturia of one or two times since the onset of his edema but there were no other symptoms noted. Because of the increasing fatigue, after ten days he consulted a physician and was immediately hospitalized.

He had never had any previous illness of significance.

His family history is irrelevant.

Physical examination showed a well-developed and nourished young man appearing quite comfortable. There was marked pitting edema of the lower extremities, penis, scrotum, sacrum and lumbar region, and puffiness of the eyelids and to a less degree of the face. The tonsils appeared to be normal. The lower teeth were quite carious and discolored; the upper teeth had been removed. The fundi were negative except for slight tortuosity of the arterioles and a physiological cupping. The heart was not enlarged and no murmurs were audible. Gallop rhythm was heard. The blood pressure was 150/110. There were scattered rare medium coarse râles over the posterior chest bilaterally. The abdomen was slightly distended and tympanitic and there was slight edema of the abdominal wall. Intraperitoneal fluid was not demonstrated clinically.

The temperature was 100.3°, the pulse 100. The respirations were 20.

The urine showed a large trace of albumin and a specific gravity of 1.032. The sediment contained 8 red blood cells, an occasional white blood cell and a few hyaline casts. Examination of the blood showed a red cell count of 4,900,000, with a hemoglobin of 80 per cent. The white cell count was 4,900, 75 per cent polymorphonuclears. A stool examination was negative. The nonprotein nitrogen of the blood was 28 milligrams per 100 cubic centimeters. The serum protein was 2.8 grams per cent. A Hinton test was negative.

He was given a diet containing a low salt content with a protein component of 80 to 100 grams per day. Although the charted intake and output exhibited moderate fluid retention the patient's edema gradually subsided. His temperature dropped to normal twenty-four hours after examination and except for transient rises to 101° to 103° following intravenous injections of typhoid vaccine (25,000,000 to 100,000,000) at scattered intervals it remained at the normal level. At the end of the first week he became nauseated and vomited each morning. This subsided after six days. During this time his white blood cell count rose to 14,000, with 84 per cent polymorphonuclears. The serum protein was now 3.97 grams per cent, the chlorides 631 milligrams per cent and the nonprotein nitrogen 38 milligrams per cent. The urine continued to show a large trace of albumin and had a specific gravity varying from 1.002 to 1.032. The sediment remained similar to that of the admission specimen. During the third week a booming quality of the second aortic sound became evident. By this time the edema had almost entirely disappeared and the patient felt much improved. At the end of one month he again began to vomit and the edema returned. The blood pressure was 135/95 and a systolic murmur was now audible over the precordium. He was given a transfusion of 500 cubic centimeters of blood with no evident change in his condition. His hair was observed to be graying quite rapidly. Ascites appeared. He was given 3 grains of thyroid daily for five days without any clinical change. His vomiting ceased within a week. During the sixth week the edema diminished slightly but examination of the fundi revealed some haziness of the discs and fullness of the veins. Diuresis was not established, nor had his edema subsided completely, but he was sent home at this time for convalescent care.

Second Admission, five weeks later.

He felt quite well for two weeks and then there was a rapid return of edema and repeated vomiting of food directly after ingestion. Two weeks before entry he began to have slight blurring of vision and twelve days later developed diarrhea.

Physical examination showed generalized anasarca. The skin was dry and coarse. The fundi showed choked discs, small patches of exudate and rare hemorrhages. There was a slight systolic murmur audible over the precordium and a moderately accentuated aortic second sound. The blood pressure was 200/145. A few me-

dium coarse râles were audible at the angles of the scapula. The abdomen was tense and distended. The scrotum was swollen to the size of a large grapefruit. There was marked clubbing of the fingers and toes, a finding which had not been recorded at his previous admission.

The temperature was 98°, the pulse 100. The respirations were 20.

The urine showed a specific gravity varying from 1.008 to 1.022. There was a slight to large trace of albumin. The sediment was similar to that reported upon his initial admission. The blood showed a red cell count of 4,500,000, with a hemoglobin of 75 per cent. The nonprotein nitrogen of the blood was 24 milligrams, the chlorides equivalent to 106 cubic centimeters N/10 chloride per 100 cubic centimeters. The serum protein was 3.5 per cent, the cholesterol 555 milligrams per cent.

The urinary output continued slightly below the fluid intake except for a slight spontaneous diuresis directly following admission and a brief induced diuresis two weeks later following the injection of salyrgan. Vomiting ceased promptly after admission. On the third day intravenous injection of typhoid vaccine (100,000,000) produced a febrile rise to 102°. During the third and fourth weeks he received three grains of thyroid daily with a subsequent gradual rise of pulse to 120. The temperature remained normal. On the twenty-eighth day he complained of diminution of hearing and left earache. A reddened drum was noted and was treated expectantly. The temperature rose to 99° but subsided promptly. Three days later he developed right earache. The right drum likewise became injected. The temperature rose to 100°. The pain and fever subsided gradually but the patient remained partially deaf. During the fifth week he again began to vomit small amounts at irregular intervals after meals. This continued for the remainder of his hospital stay. On the thirty-fourth day the blood pressure was 160/120. The eyegrounds were unchanged. The edema was still marked. He was drowsy at times but for the most part was quite cheerful. The white blood cell count was 20,000. The specific gravity of the urine now remained between 1.007 and 1.015, with a single specimen showing a specific gravity of 1.020. The nonprotein nitrogen was 31. He was discharged on the forty-ninth day with little evident improvement.

Final Admission, a month and a half later. There had been no change in his condition until two weeks before entry. At this time his physician did an abdominal paracentesis. A few days later he developed a sharp pain in the right loin which radiated to the kidney region. This usually occurred after meals and was relieved by a sedative.

The patient had a pasty yellow face. The abdomen was huge and there was massive generalized edema. Examination of the fundi showed slight haziness of the discs medially. There were some small hemorrhages and many whitish yellow exudates. The vessels were not remarkable. The tongue was dry. There was flatness over the lower half of both lungs posteriorly with absent tactile fremitus. Some bronchial breathing was audible in the area of dullness and was more marked on the left where egophony was also present. The heart was not enlarged and there was a rough to-and-fro friction sound heard best over the mitral area. The heart sounds were distant. The blood pressure was 125/105. A fluid wave was demonstrated in the abdomen.

Examination of the urine showed no change from the specimen previously examined. The blood showed a red cell count of 3,290,000, with a hemoglobin of 60 per cent. The white cell count was 12,300, 74 per cent polymorphonuclears. A second abdominal paracentesis was done in which 7,500 cubic centimeters of fluid was removed. The specific gravity was 1.006, the total cell count 57 per cubic millimeter, red blood cells 29 per cent, lymphocytes 47 per cent.

Because of nausea and a capricious appetite the patient was permitted to eat and drink whatever he chose. There was no change in his general condition. During the third week another abdominal tap was done. The specific gravity was 1.002. Chlorides were equivalent to 90 cubic centimeters of N/10 sodium chloride per 100 cubic centimeters. The total protein was .8 per cent, the cholesterol was 36 milligrams per 100 cubic centimeters. There was little change in the cell content. During the fourth week the plasma proteins were 4.2 grams per cent. The nonprotein nitrogen was 49 milligrams. The chlorides were equivalent to 84 cubic centimeters N/10 chloride. Because of restlessness he was given morphin. During the fifth week his respirations were between 6 and 10 per minute. He became progressively more drowsy and at the end of the sixth week, eight months after the onset of his symptoms, went into coma and died.

Differential Diagnosis

Dr. Myles P. Baker: To single out a few of the more significant findings here, if we are dealing, as I suspect, with a case of Bright's disease,—chronic glomerulonephritis,—the appearance of the edema three days after the patient had had sore throat with nasal discharge is interesting and important, although the exact nature of the association remains decidedly in doubt. As a rule the appearance of edema as early as two or three days after the upper respiratory tract infection is more indicative of an exacerbation of glomerulonephritis than an

initial attack, in which the period between onset of tonsillitis or sinusitis, and the like, and the appearance of symptoms of nephritis is more often as long as a week or two weeks; ten days perhaps is the average.

The statement of slight non-productive cough is interesting. It may be only an impression on my part but it seems to me that most of the few such cases that I have seen beginning with stubborn edema, presenting edema as the main complaint, have this irritative cough, perhaps definite moist râles at the bases, evidences of an ill-resisted bronchial infection.

The nocturia of one or two times since the onset of the edema I hesitate to comment on, as no further mention is made of it. It seems hardly likely that this is the beginning of a compensatory polyuria with renal insufficiency because we have no other proof of that at the moment.

Slight tortuosity of the arterioles in the fundi is an equivocal finding, but does bear out our impression that this man has had an insidiously developing renal lesion, for some time antedating the appearance of his symptoms. I think that, too, is borne out by the finding of the low level of serum protein, 2.8 grams per cent. It seems hardly likely that this level would be reached in such a short period of time as his symptoms would indicate. Presumably he had a marked proteinuria for some time, largely albumin, and that had led to this depletion of serum protein.

The urinary findings mentioned at this point are important here because they are the only specific mention we have of examination of the urine sediment. He has microscopic hematuria, a few white cells, which one would expect in this type of Bright's disease, and only a few hyaline casts. One generally finds in association with such marked proteinuria as this man has fatty granular casts with, frequently, doubly refractile lipoid bodies in the urine sediment. The white blood cell count is such as you would see particularly after an upper respiratory tract infection; 75 per cent polymorphonuclears are consistent with secondary infection,—bronchitis, tracheitis and so on.

This episode lasting a week, of nausea and vomiting, with leucocytosis, is unexplained. One wonders if there has been a recrudescence of upper respiratory infection, but we do not know. One wonders in such a case whether there is active poorly resisted pneumococcus infection in an ethmoid sinus, for instance.

We have evidence of retained ability to concentrate the urine, and a suggestion that such gallop rhythm as was observed on admission was the result of some cardiac dilatation such as occurs with an acute phase of glomerular nephritis; and the booming quality of the aortic second sound indicates a more satisfactory cardiac function.

No attempt was made to treat his tonsils by radiation or surgery; nor have we any evidence that throat cultures were done. As a rule figures bear out the clinical impression that this type of nephritic does not respond well to tonsillectomy. One would hesitate not to treat pus under pressure in the sinuses, or tonsils around which there had been a peritonsillar abscess on their own merit. But a hunt for some focus of infection and eradication on vague indications does not help this type of unremittingly edematous individual. Theirs appears to be a mediocre immune reaction, unimproved by, let us say, tonsillectomy.

One wonders on the second admission how close this patient came to some cerebral episode such as has been described under the general heading of hypertensive encephalopathy with this marked rise in blood pressure and evidence of hypertensive neuroretinopathy.

"He was given three grains of thyroid daily for five days without any clinical change." The pulse rate later increased. That is rather unusual. Usually most of these patients tolerate large doses of thyroid without any apparent tachycardia.

DR. WYMAN RICHARDSON: I do not think that was right. He got up to twelve or fourteen grains a day.

DR. BAKER: This second admission was punctuated after he had been in the hospital for four weeks by mild otitis media. He continues to have high blood pressure and the leucocytosis often seen in these cases. He is beginning to show difficulty in concentrating his urine, indicating fewer and fewer functioning glomerulotubular units.

The physical findings on the third admission are interesting. They are consistent with fluid at both bases. The signs on the left make one wonder whether the man has a pericardial effusion, to which in some degree he is entitled with his general anasarca. To-and-fro friction sounds heard over the mitral area may be the first evidence of a fibrinous pericarditis with fluid in both pleural cavities. It may be a pleuropericardial rub. The distant heart sounds, the lowered pulse pressure and the lowered systolic pressure speak for fluid in the pericardial sac, or cardiac dilatation.

Examination of the urine showed no change from the specimens previously examined.

There is a high chloride content in the ascitic fluid, I believe a rather characteristic finding in these cases. The total protein is a little high for such a so-called "nephrotic" fluid.

This man has been through most of the trials and tribulations of the essentially edematous nephritic, as Dr. O'Hare chooses to call such a case. As far as differential diagnosis is concerned it seems to me highly unlikely that we are dealing with any other disease than progressive glomerulonephritis. One wonders about the possibility of amyloid disease but

amyloid disease in the presence of such definite hypertension and hypertensive neuroretinopathy as this man has must be a very rare finding. Amyloid disease does occur without any obvious focus for sepsis; but I think we can exclude it here as a most unlikely possibility. This man has had on physical examination definite signs of arterial damage and I take it that it is probable that his kidneys will show not only marked evidence of glomerulitis and tubular degeneration but also arteriolarsclerosis, which may have contributed to the rather rapid tempo of his disease. I think it is quite likely that his kidneys will be fairly normal in size, perhaps the slightly swollen, large, pale kidney of essentially edematous nephritis.

DR. TRACY B. MALLORY: Dr. Richardson, you saw this patient on the ward. Have you anything to add?

DR. RICHARDSON: In the first place I am not sure he had clubbed fingers. I think they were very likely the hereditary type. When I first saw him he had fingernails that curved in both directions.

From the point of view of treatment, one of the most difficult symptoms were the attacks of severe pain in the right epigastrium, not in the right loin, coming on after eating at the time when he had marked ascites. It was very severe pain requiring a large dose of morphia for relief. I do not know now what the cause of this pain was; unless, associated with edema in the gastrointestinal tract, it was possibly some temporary obstruction.

In regard to the treatment, there is probably some question why typhoid vaccine was used in this patient. It was, I thought, a brilliant idea of mine on the basis of previous patients I had seen; one in particular who developed an acute appendix when he was edematous with this disease. The appendix ruptured, operation being impossible, and he developed an appendix abscess and had a high swinging temperature, whereupon he had the most tremendous diuresis I have ever seen. When the nephrosis cleared temporarily, the surgeons went in and drained the abscess and he was well for a number of years. So when we discovered that this patient could not take a high protein diet—I did not feel very brave about the acacia intravenously that we hear about; it does not seem to me that the reports are very encouraging,—and since we could not transfuse him frequently we did try the typhoid and if you look at the chart with hopeful eyes you will see an increase in output of 50 to 100 per cent, temporary improvement that was not lasting.

I did not see him during the last month of his illness, but up to the time I left I did not think he had any pericarditis or pericardial fluid. I agree with the diagnosis that Dr. Baker has made, although in the beginning I was inclined to think it was subacute. I agree that it was long-standing glomerulonephritis with acute exacerbation at the end.

About the tonsils, I again could not get very enthusiastic about fooling around in the throat although the tonsils did look infected.

DR. J. H. MEANS: I was interested in the last note, the statement that the tongue was dry when he was water-logged. I think that is an interesting relationship and one we see not infrequently. He was dehydrated and water-logged at the same time. I remember a patient a year ago with a somewhat similar picture of dropsy and cerebral symptoms that could have been uremic or something else but the tongue was very dry indeed. He was given intravenous fluid in spite of his edema with marked improvement and marked diuresis.

I think the therapeutics are more interesting than the diagnosis, which does not interest me very much. The therapeutics are extremely complicated and we are very much in the dark about what to do with people of this sort. There is nothing in this history to tell what was done about fluid. It speaks of fluid balance but it does not say whether fluids were given freely or withheld except in the last paragraph where it says he was permitted to drink what he chose. I often think that letting the patient drink what he chooses is the best thing to do because nature knows more about what the body needs in the way of fluids than the doctor.

DR. RICHARDSON: In regard to fluids by mouth, we could not get much into him. For long periods we gave large amounts of glucose by vein with a low salt diet. At the time of the first entry he had a high blood chloride.

DR. MEANS: When you gave him intravenous fluids what happened to the fluid output? Did it give him a diuresis?

DR. RICHARDSON: I do not think it did. It improved his general condition but the charted output did not show much change.

DR. MEANS: What did the thyroid do in the way of producing diuresis?

DR. RICHARDSON: Nothing. I think he got up to fourteen grains a day.

DR. MEANS: That is a colossal dose if it is USP thyroid.

CLINICAL DIAGNOSIS

Chronic nephritis with edema.

DR. MYLES P. BAKER'S DIAGNOSIS

Early chronic glomerulonephritis, with edema.

ANATOMIC DIAGNOSES

Subacute glomerulonephritis.
Multiple septic infarcts of the lungs.
Hydrothorax, bilateral.
Ascites.
Sterile peritonitis.

Pathologic Discussion

Dr. Mallory: The kidneys here were essentially normal in size, weighing 270 grams, perhaps small for a man, but he was a small individual and all the other organs were proportionate. Grossly they were smooth and pale, consistent with a subacute nephritis or nephrosis. Microscopically there is a quite typical intercapillary glomerulonephritis. The tubules show comparatively little degeneration. The average case of Bright's disease with marked edema will show generally a pretty marked fatty degeneration of the tubules, but one can see the entire syndrome of nephrosis with absolutely negative tubules and changes apparently limited to the glomeruli.

The other point which Dr. Baker raised in the differential diagnosis, as to how long this process had been going on, is not possible to settle exactly. It is a very common experience that the first symptom noted by a patient with Bright's disease comes at the very terminal stage, a few weeks or months before death, in an illness that later pathologic examination assures has been in existence for years, and it is almost always safe to bet that a case of nephritis is considerably more chronic than the clinical history might indicate. However, in this case I do not think that was true. The kidneys had not shrunken to a significant degree. There were very few completely sclerosed glomeruli and few changes in the blood vessels.

The heart was somewhat small in size, certainly no hypertrophy at all. There was no evidence of pericarditis.

The terminal pulmonic signs turned out to be emboli rather than bronchopneumonia. There was one rather large area of infarction and there were two quite small septic foci in the upper lobes with beginning abscess formation which I feel were septic infarcts.

A Physician: Was there anything in the gastrointestinal tract?

Dr. Mallory: Absolutely nothing.

Dr. Baker: Was the intestine edematous?

Dr. Mallory: Not noticeably so.

Dr. Baker: Do you think that diarrhea could be caused by edematous intestine?

Dr. Mallory: Diarrhea in the terminal stage of nephritis is usually associated with typical uremic colitis, but he did not have it.

A Physician: Did you find a focus for the emboli?

Dr. Mallory: No.

I neglected to mention that the peritoneal fluid at the time of autopsy was slightly hemorrhagic and somewhat turbid. It impressed us as a sterile peritonitis following hemorrhage at the last tap rather than an acute infectious peritonitis.

Dr. Baker: I would like to report that the patient whose history Dr. Richardson cited has been coming back to the Outpatient Department from time to time and now, four years after his serious illness, has no signs of even a latent glomerulonephritis. The sediment is entirely normal as far as we know, without doing Addis counts. There is no active renal lesion. After he left the surgical wards the first time he had to return two months later for treatment of a subdiaphragmatic abscess; and he was very sick for two or three months, but he has never had any return of edema.

A Physician: I should like to ask about the sediment of the urine in today's case.

Dr. Baker: It tallied with Dr. Mallory's findings,—less evidence of tubular damage than one would expect in such an individual.

CASE 21472

Presentation of Case

A sixty-four year old white native farmer was admitted complaining of abdominal pain, loss of weight and malaise.

One year before entry the patient had an attack of frequent loose watery bowel movements which continued for ten days. At this time he observed that his weight, which had been 200 pounds four years previously, had decreased to 174. This had followed no dietary restrictions or other known etiological factor. Following the cessation of the attack of diarrhea the patient continued to feel run-down and after three months consulted his physician who prescribed a diet and a tonic. He was told to avoid fatty foods. There was no improvement in his condition and he developed "chafing" pains in his right upper quadrant which caused him to lift his clothes from the involved area for relief. This recurred irregularly, often seven to eight times daily and then not at all for several days. These pains continued with little change up to his admission. For a year he had also suffered from cramplike pains in the lower abdomen which usually began one and a half hours after his noonday meal and often aroused him from his afternoon nap. The distress was promptly relieved by a teaspoonful of milk of magnesia but recurred at almost daily intervals. Two months before admission the patient made several visits to a clinic where x-ray studies of the gall bladder and gastrointestinal tract were negative except for the presence of diverticula along the sigmoid. He was also told that he had high blood pressure. At no time was there nausea, anorexia, vomiting or noticeable melena. His bowels moved regularly daily after his initial attack of diarrhea. He had developed a nocturia of three times during his illness. His weight had decreased to 151 pounds.

His father died at the age of sixty-eight of pneumonia, his mother at eighty-four of shock.

Several members of his father's family had had tuberculosis.

He had had typhoid fever but no other illnesses of significance.

Physical examination showed a well-developed and nourished elderly man who appeared to be comfortable. His thyroid was enlarged and firm. The heart was enlarged to the left and a systolic murmur was audible. A_2 was greater than P_2. The blood pressure was 220/110. The remainder of the physical examination was reported as being negative.

The temperature was 99.6°, the pulse 75. The respirations were 20.

Examination of the urine was negative. The blood showed a red cell count of 3,300,000, with a hemoglobin of 55 per cent. The white cell count was 18,500, 72 per cent polymorphonuclears, 13 lymphocytes, 13 monocytes, 2 eosinophils. The platelets were reported as being normal. The stools repeatedly gave a strongly positive reaction to the guaiac test but were otherwise negative. A Hinton test was negative. The nonprotein nitrogen of the blood was 30 milligrams. The basal metabolic rate was +18 per cent. Analysis of the gastric content showed a free hydrochloric acid of 0 to 9 and a total acid of 3 to 15. The reaction to the guaiac test was negative. An electrocardiogram showed left bundle branch block.

A barium enema passed through the ileocecal valve without delay. There were a few small diverticula in the sigmoid. There was no evidence of spasm and the bowel emptied moderately well with defecation. A gastrointestinal series showed a small hernia of the stomach through the esophageal hiatus. The first part of the duodenum was long and the second part short. Some of the loops of the small intestine appeared to be slightly dilated but there was no evidence of any intraluminal disease.

Proctoscopy was done shortly after admission but no pathologic process was found up to a point 14 centimeters from the anus. The stools continued to react positively for microscopic blood and occasionally showed fairly large amounts of macroscopic blood. He remained in the hospital for one week and then returned to his home. Four days later he was readmitted stating that although his bowels had moved once daily they had been tarry in appearance and on that day they had been quite copious and fluid in character. He became weak and had frequent dizzy spells. Transfusion was given on the following day and two days later a laparotomy was done.

Differential Diagnosis

Dr. Leland S. McKittrick: This man of sixty-four had apparently been sick for about one year and his initial symptom, as near as one can tell, was an attack of frequent, loose, watery bowel movements lasting ten days. Associated with this he first noticed loss of weight of twenty-six pounds, but he had not been weighed for the previous four years. There is nothing about the first attack of loose watery bowel movements which gives me any lead as to just why he had it. Presumably there was no gross blood. He did not have a complete recovery following cessation of diarrhea and that, presumably, can be taken as the beginning of this present illness. He had with that this "chafing pain" in the right upper quadrant. He has had cramp-like pain in the lower abdomen and the striking thing about this pain is that it comes pretty regularly an hour and a half after the noonday meal and is relieved by milk of magnesia. It is my impression that not infrequently a patient, particularly beyond middle age, may refer the pain of a posterior wall ulcer to the lower abdomen or elsewhere. That is, he may not be definite about the location. The constant regularity with which it recurs and the fact that it is relieved by milk of magnesia may be of some significance. Later the x-rays were negative. That makes duodenal ulcer unlikely but does not exclude it, particularly if it were a posterior wall one.

He had no more vomiting or diarrhea but he continued to lose weight, having lost a total of forty-nine pounds. There is nothing in the history up to this time that makes it possible for me to draw any definite conclusions as to what is the matter with him. His family history is negative. I do not believe the past history of typhoid means a great deal. He has an enlarged firm thyroid which I think is not significant. He does have, apparently, cardiovascular disease. He has an enlarged heart, a hypertension of 220/110. He is essentially afebrile. He has a perfectly good pulse. On the laboratory side he has a pretty marked secondary anemia, also a leucocytosis, both actual and relative, that is a polymorphonuclear increase. His blood is apparently normal from the point of view of platelets and there is nothing to enable them to say he was bleeding because of any blood disease. He has a persistently positive guaiac in the stools and at times he has gross macroscopic blood. In his vomitus where the hydrochloric acid is low he has a persistently negative guaiac. Therefore, it would seem to me that we can discount his stomach as having anything to do with the hemorrhage. More than that, it would seem at present that large quantities of macroscopic blood point pretty definitely to the fact that the blood must be lower down than the small bowel. I think it is possible for active hemorrhage from the upper bowel to come out of the rectum as macroscopic blood but it does not occur very often, and I never had seen it. Therefore, it seems to me that it must be coming from the large bowel.

A barium enema was negative except for a few diverticula of the sigmoid. We cannot accept these as having anything to do with the hemorrhage.

The diaphragmatic hernia I think can be passed by. There are occasional cases of secondary anemia associated with diaphragmatic hernia but I think in this instance that that cannot be a factor because of the negative guaiac in the stomach contents and positive guaiac and the gross blood by rectum.

The proctoscopy was negative for a distance of fourteen centimeters. It does not say why it was not passed higher or whether there was any blood in the rectum at that time. I do not think the statement of a negative proctoscopy is particularly helpful to a person who is trying to interpret it; but I might assume from the negative proctoscopy that they saw nothing in the mucous membrane or any evidence of blood, either localized or coming down from above.

DR. RICHARD H. SWEET: That is correct.

DR. MCKITTRICK: The association of bloody diarrhea and abdominal cramps of course brings several things to mind immediately. At least one of them is ulcerative colitis. I believe a negative x-ray and negative proctoscopy exclude ulcerative colitis. Carcinoma of the large bowel has not been excluded. It is perfectly possible and surely not at all unlikely to have a carcinoma of the large bowel in the absence of a positive x-ray. Carcinoma of the hepatic flexure particularly may not show by x-ray. On the other hand, about eighty per cent of lesions in this location have a palpable mass and a negative x-ray plus absence of a palpable mass make this unlikely. The proctoscope did not get high enough to exclude another blind area 18 centimeters up, which is the common site for polypi and cancer and difficult to visualize by x-ray. In other words, I am not able at this time to make what to myself is a satisfactory diagnosis in this instance, but I cannot exclude a lesion of the rectosigmoid.

He has cardiovascular disease. I do not believe that a mesenteric thrombosis can very satisfactorily give this picture.

Therefore, I am forced to leave this today without a definite diagnosis except to say that I believe his bleeding is from the large bowel. I do not think he has a carcinoma. I do not believe he has a diffuse polyposis and I feel very sure that he does not have an ulcerative colitis.

X-RAY INTERPRETATION

DR. AUBREY O. HAMPTON: This is the chest film. It is practically normal except for enlargement of the heart and calcification in the midlung field. There is no enlargement of the glands and nothing to suggest malignancy. I did not fluoroscope this patient but these films of the stomach show nothing abnormal except for this small hiatus hernia through the diaphragm. I think the variation in the length of the duodenum was probably due to pressure from the colon upon the stomach displacing it upward. This hernia of the stomach is the commonest type of hernia and is surprisingly common in old people. It is probably normal. The barium enema filled the colon perfectly satisfactorily. It is a little bit dilated in the proximal portion. The evacuation is not quite so complete as usual but certainly the dilatation did not persist. You cannot say he had an obstruction. In this film you get the impression that the spleen is enlarged. Here is the mucosal relief of the sigmoid just proximal to the rectosigmoid and it is perfectly normal except for this diverticulum-like pouch.

CLINICAL DISCUSSION

DR. TRACY B. MALLORY: Dr. McKittrick has left the case wide open.

A PHYSICIAN: How about bleeding from Meckel's diverticulum. Would that be possible?

DR. ARTHUR W. ALLEN: Would he not have had that earlier in life?

DR. DANIEL F. JONES: Several things might clarify it a little. In the first place he had pain one and a half hours after meals which is about the time for pain in large intestine obstruction. He had blood in the stools constantly. He had irregular bowel movements, mostly diarrhea. The textbooks talk about constipation in carcinoma of the rectum. The surgeon rarely sees patients with constipation in cases of carcinoma of the rectum. It is much more often with frequent loose movements. I think that if many physicians could get that into their minds they would not go astray on so many cases. By the time patients get to the surgeon they have diarrhea, which is a very improper term to use. The patients themselves rarely admit that they have diarrhea. They do have anywhere from five to twenty-five episodes a day when they have to go to stool to get rid of a little gas, mucus or blood and frequently very little stool, so that the word diarrhea is a very improper term to use to the patient. You have to talk the language of the patient in order to find out what he means. Now that puts it very definitely, it seems to me, in the large intestine. That might be a polyp or malignancy. Polypi would frequently cause diarrhea or frequent movements without any great amount of obstruction but you must account for some obstruction here by the frequency with which he has pain. It is true that you occasionally get pain in the lower abdomen from an ulcer but that is much more frequently due to a gastroduodenal ulcer than an ordinary gastric ulcer or ordinary duodenal ulcer.

As to proctoscopy, I should like to say that

in a man with a loss of weight and diarrhea and pain I do not think it is fair to say that the proctoscopic examination is negative when you go only 14 centimeters, because 18 centimeters, as Dr. McKittrick said, is the most frequent site for a polyp and if you are going to use a proctoscope you should at least go up to the rectosigmoid junction because that is the difficult place to see a growth by x-ray and it is a little difficult to get by also with a proctoscope. If he cannot get by this region the surgeon should know why.

As to diverticulitis and bleeding, I think that it is a very important question. I think you should not consider that diverticulitis causes bleeding. It does have a little blood occasionally. I am not sure of the figures but the only records that I have seen state that there is a little blood in five or six per cent; so that you cannot go much on that and you ought not to in this man because he has lost so much weight, from two hundred pounds down to one hundred and seventy-four.

I do not know about arterial disease but I think that it very rarely gives pain regularly after each meal. Therefore, I do not think it can be due to arterial disease. Occasionally these people lose weight. It would not be likely that a patient would lose as much as this man, so that I think that it is much more likely that this is a carcinoma or malignant disease of the colon or a polyp.

Dr. Sweet: There are two or three facts in the history that Dr. McKittrick should have had. As it is, he certainly made an admirable job of his discussion. The man was sent in with the diagnosis of probable undulant fever because the outstanding symptom was recurrent attacks of chills and fever. He had been to several other doctors. One had treated him with emetin. Every few weeks he had a spell of fever with chills, the last persisting attack of fever and chills was about three weeks before he came in here. We could not make a diagnosis. Incidentally, he had had no bleeding from the rectum until after he came into the hospital and then he had a massive hemorrhage on the day following proctoscopic examination. It is not fair to say that the proctoscopy was negative. The reason I could not get beyond fourteen centimeters was that there was something which seemed to be outside of the bowel which made it impossible to turn the corner of the sigmoid. The x-ray had shown us that he had diverticula and I thought he might have an inflammatory mass resulting from that which made it impossible to get around it. There was no sign of polyp or tumor and no blood was seen.

One other interesting point which Dr. Schatzki brought out was that he had several dilated coils of intestine in the x-ray. Another point in the history was that he had had two definite attacks suggesting bowel obstruction during the preceding year with vomiting and acute illness, one attack lasting four days.

At operation we found a tumor of the sigmoid which I thought of course was carcinoma. This had perforated and caused a local abscess in the pelvis, not a large abscess, however. It also perforated into the ileum and he had a fistula between his ileum, about eight or ten inches above the ileocecal valve, and the sigmoid. I wonder if the fact that he passed tarry stools was not due to bleeding from the ileal side of the fistula so that the blood went around the colon and thus to the rectum rather than directly down the rectum, in which case the blood should have been bright red.

Preoperative Diagnosis

Intestinal hemorrhage.

Dr. Leland S. McKittrick's Diagnosis

Hemorrhage from colon — cause undetermined.

Pathologic Diagnosis

Lymphoblastoma, sarcomatous type.

Pathologic Discussion

Dr. Mallory: The examination of this tumor showed that it was not carcinoma but a lymphosarcoma. The great majority of the tumor lies in the outer layers of the wall of both the sigmoid and the ileum, the mucosa being relatively free in each instance. I do not find it possible to say with certainty from the specimen in which of the two structures it originated, although there was more tumor present in the sigmoid than the small intestine. The patient recovered from the operation and is still under observation.

Dr. Sweet: He now has a palpable spleen and a very abnormal blood picture which Dr. Hunter thinks is rather suggestive of early lymphatic leukemia. His polymorphonuclear count is down to twenty and he has a lot of abnormal lymphocytic series cells in his blood.

Dr. Jones: May I say that it is not fair to say that the proctoscopic examination was negative. I want to call it to your attention that errors are made with a proctoscope very often because the examiner does not feel with the end of the proctoscope. It is a perfectly legitimate thing to do.

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CLINICAL APPLICATIONS OF HETEROPHILE ANTIGENS AND ANTIBODIES

UNTIL quite recently, the terms, heterophile antigen and antibody, were used by only the most erudite of immunologists. The latter term was applied to the nonspecific antibody produced by the injection of certain bloods or organ and tissue extracts into certain animals, a phenomenon originally described by Forssman in 1911, who demonstrated the presence of anti-sheep hemolysins in the sera of rabbits that had been injected with guinea pig organ extracts. The antigens capable of producing such antibodies are contained in the organ and tissue extracts of guinea pigs, horses, mice and pigeons and in the bloods of sheep and goats. They are absent in another group of animals, including rabbits, cattle, pigs and rats, and in these animals heterophile antibodies can be produced by the injection of the antigen. Man is peculiar, as the antibodies are present or can be developed even though the antigen has been demonstrated in red blood cells of groups A and AB. More recent work has shown that the antigen is present in certain bacteria, such as members of the typhoid-paratyphoid-dysentery group and pneumococci.

Heterophile antibodies can usually be demonstrated in the sera of normal human beings, but, when present, are in very low concentrations. In certain diseases, notably infectious mononucleosis and certain blood dyscrasias, it has recently been shown that such antibodies are markedly increased. So much so, in fact, that the demonstration of anti-sheep hemolysins in high dilutions of freshly obtained serum from a suspected case of infectious mononucleosis practically confirms the diagnosis.

The practicing physician is now confronted with a prophylactic and a therapeutic procedure, both of which have been developed on the assumption that the presence of such antibodies, either produced actively by the administration of the antigen or injected passively, is of the utmost significance.

The first is an oral vaccine which has been recommended[1, 2] as a prophylactic agent against the common cold. The active constituents of this vaccine consist of the dried bodies of an avirulent, non type specific pneumococcus, containing heterophile antigen, and a hemolytic mouse virulent streptococcus. In the clinical report, 462 vaccinated individuals showed a decrease of 57 per cent in the number of colds for the *school* year as compared with the average number per year for the preceding three years, whereas the 527 controls showed a decrease of only 12 per cent. Among 30 carefully studied cases, the development of appreciable heterophile antibody titer was associated with almost complete immunity. In spite of such excellent results, one must be extremely cautious in adopting such a procedure until more confirmatory evidence has been presented. One should not forget that the probable etiologic agent of the common cold is a virus, that parenteral injection of most vaccines is more efficient than oral administration and that even the parenteral injection of vaccines for the common cold is of distinctly questionable benefit.

The second is the addition of heterophile antibody to antipneumococcic serum[3]. On the basis of the stated, but not necessarily proved, facts that horse serum and pneumococci contain heterophile antigen, that union of these antigens with the protective heterophile antibodies in the patient diminishes the efficacy of such antibodies and may produce untoward reactions and that such sera have been proved to be more effective (in rabbits), it is claimed that the preliminary treatment of antipneumococcic horse sera with heterophile antibodies and their addition to such treated sera result in a product which gives fewer reactions and may be used against all infecting types. Finland, Ruegsegger and Felton[4] have justly criticized these theoretical claims, after having failed to show that heterophile antibody has any relationship to

the course or outcome in human cases of pneumococcic pneumonia[5]. They question the contention that this serum is less toxic. They call attention to the fact that advances in the serum therapy of pneumococcic pneumonia can be attributed to the results obtained in cases treated with adequate amounts of homologous serum. If the claims made for the serum containing heterophile antibody are accepted, they believe that a certain number of patients will fail to receive sufficient amounts of homologous antibody, because of the absence of "typing", and others will be exposed, unnecessarily, to the hazards of administration and the expense of a serum of questionable potency. They acknowledge that their opinions are not based on direct observation of the use of fortified sera and rightly conclude that such observations, in the last analysis, furnish the final criteria on which the use or discard of this product should depend.

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THE SOCIALIZATION OF MEDICINE

WHAT is this socialization of medicine of which so much is said, and of which so little is actually thought through? One does not get a very clear idea from the views expressed. Something is going on in medicine, some important change is taking place, and we are on our way, although we do not know whither the path will lead us. It is said also that physicians are backward, even blind, in failing to recognize this inevitable progress and adapt to it themselves and their practice.

Socialization of medicine means to make medicine conform to the principles of socialism. Since the socialists, perhaps most of all, fail to agree as to the principles of socialism, how can others be expected to know what it is all about?

Socialism and individualism are permanent tendencies in human nature; as an ultimate philosophy either is inadequate and so misleading. In the division of labor, it has been found expedient to have certain functions ultimately controlled by society at large, directly controlled by society organized politically, that is to say by the government. These functions are performed for the whole by the parts. Under complete and perfect socialism, if such there be, the government controls and directs every part. The question as to whether a function is or is not performed socialistically is settled by the answer to the questions: Who directly pays the bill? Who directly controls the group? Of course, in the long run society pays the bill in any case. It is to be remembered that a given socialistic scheme is not intrinsically better because it is socialistic; neither is it intrinsically worse. The outcome can be determined only by experiment. The method of science includes controlled experiment. It is true that history repeats itself; but never quite exactly.

Education is one of the socialistic enterprises to which we are committed. There are students of education, however, who think that our very commitment to this socialistic enterprise has made more imperative than ever the need of our continuing to develop our private educational system.

The question at issue in medicine does not concern primarily the quality of medical service. That is to say, it is not that the science and art of medicine are so far behind what one has a right to expect. It is a fact that the science of medicine has progressed so far, and that the art of medicine has become so complicated and thus so expensive that the average citizen cannot pay the cost for all medical services out of his own resources. The socialization of medicine means that the cost of medical care should be met by the government and not by the individual. Control goes to the person or organization responsible for the payment of the bill.

Again and again we have found that the governmental hand has had a paralyzing influence. Indeed so often has this been true that many persons look askance at the injection of the government into any undertaking. If mere quality of service, dollar for dollar, is considered, is there anything the government does that would not be done better by private competitive enterprise?

Yet many times it has seemed wise, even necessary, to have the government interpose—to protect the weak against the strong, the poor against the rich, the ignorant against the knowing. Is there any justification besides protection?

What justification is there for the socialization of medicine? Against whom do the sick need to be protected? Is it against the medical profession?

If it has been expedient, perhaps necessary, to socialize medicine in some fields, to protect the well against the sick, and the poor and the ignorant against themselves, is not this the best of reasons why medicine should not be wholly socialized, why more vigorous efforts than ever should be made to preserve part of it, at least, from the dry rot of governmental influence?

THIS WEEK'S ISSUE

CONTAINS articles by the following named authors:

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LEVINE, SAMUEL A. A.B., M.D. Harvard University Medical School 1914. Assistant Professor of Medicine, Harvard University Medical School. Senior Associate Physician, Peter Bent Brigham Hospital. Address: 270 Commonwealth Avenue, Boston. Their subject is "Systolic Gallop Rhythm: A Clinical Study." Page 1021.

PHILLIPS, RICHARD BETTS. A.B., M.D. University of Edinburgh Faculty of Medicine 1933. Junior Assistant Surgeon, Department of Gynecology, Boston Dispensary. Assistant in Obstetrics and Gynecology, Boston City Hospital, Out-Patient Department. His subject is "Theelin Therapy in the Treatment of Vulvovaginitis." Page 1026. Address: 270 Commonwealth Avenue, Boston.

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ROBERT HOOKE, 1635-1703

THE subject of this biographical sketch was one of the remarkable geniuses of the 17th Century, in a general way comparable in its diversity and imaginative foundation to the genius of Leonardo da Vinci. He lacked, however, that very essential quality of mind which enables a versatile individual to "follow through" in his strokes of genius. This may perhaps have been due to the multiplicity of ideas that were always crowding each other in his mind and demanding attention. To have originated, as he claims to have done, a hundred new inventions within an average lifetime, he might well be excused if some details were left incomplete. Besides the discoveries that may unquestionably be credited to him, he provided a clue to many another that was later recorded by some other observer. The intense mental activity that characterized his entire career should have had a more robust physical background than he seems to have possessed. In early youth, on account of his lack of physical stamina and the persistent headaches from which he suffered, he was regarded as poor material for the life of study that his quickness of wit seemed to entitle him to pursue. In view of the turn his mind took when left to itself, it would seem that science might have suffered more than the church would have benefited, had he been made to follow the course originally blocked out for him by his father, the Reverend John Hooke, who was minister to the parish of Freshwater on the Isle of Wight.

It was here that Robert Hooke was born on the 18th of July 1635. Interest in him from a medical viewpoint rests upon his activities in the Royal Society, that distinguished body of scientists whose approbation all research workers in whatever field of science sought. After his father's death in 1648, he took the 100£ left him by will and went up to London at the age of thirteen where for a short time he was a pupil of Sir Peter Lely. Later he entered Westminster School and lived in the house of Dr. Busby. Here he manifested some of that intellectual precocity so frequently an accompaniment of genius. He acquired Latin, Greek and some Hebrew and other oriental languages, mastered six books of Euclid in one week, and of his own volition learned to play twenty lessons on the organ and "invented thirty several ways of flying".

In 1653, at the age of eighteen, he was enrolled at Christ Church, Oxford, as a chorister. He secured his M.A. Degree upon the recommendation of the Chancellor of the University in 1663. Because of his aptitude for mechanics he made the acquaintance of many prominent

men at Oxford and was enabled to pursue his studies in Astronomy and Chemistry. Proficiency in the latter resulted in his becoming associated with Robert Boyle whom he assisted to perfect his air pump. He worked with him until released to become the curator of experiments for the Royal Society as a recognition of a communication of his upon capillary attraction. He was elected a Fellow of the Royal Society in 1663 and later in the year became custodian of its collections, an office that later he was chosen to fill permanently, on a salary with quarters which he occupied during the remainder of his life. His income was supplemented by appointment to a lectureship in the Society, the subjects upon which he was to lecture to be determined by the Society. In 1665, he was appointed Professor of Geometry in Gresham College and, as locum tenens for Dr. Pope, he gave the lectures in Astronomy for two sessions.

He became greatly interested in respiration, combustion, the laws of falling bodies, specific weights, diving bells, land transportation, telegraphy and the relationship of barometrical readings to changes in the weather. In reference to many of these matters, his results were inconclusive but his interest in them indicates the activity of his mental processes.

He contributed to the methods of measuring time by inventing a machine to fashion the teeth of watch wheels and by measuring the variations of swinging pendulums. He published his *Micrographia* in 1665 in which were recorded numerous curious and interesting observations many of which were anticipatory of knowledge later to be more definitely established. Among them was a theory of light which he regarded as a "short, vibrative motion". Heat, also, he conceived of as being a property of matter dependent upon the vibration of its composite particles. He anticipated Mayow's conception of the nature of combustion by eleven years.

In a paper on gravity, the force of which he showed could be measured by the oscillations of a pendulum, and in a subsequent communication on curvilinear motion, offered a demonstration of the fact that the center of gravity of the earth and the moon is a point that describes an ellipse about the sun. He declared that the movements of planetary bodies are problems in mechanics.

He invented the first screw-divided quadrant and an anemometer of a form that, up to quite recently at least, was regarded as adapted for universal use. At about this same time, he devised a "weatherclock" and applied the principle of the circular pendulum to watches. He submitted himself to experimental study in an exhausted receiver and found time to give lectures on the nature of earthquakes. In 1667, he prepared a model to illustrate the rebuilding of the city of London after the great fire but his plan was not accepted though it procured for him a lucrative position as city surveyor. Several thousand pounds, accumulated through his activities as a surveyor, were found in a chest after his death. He designed a number of public buildings. By some, he is regarded as the originator of the biological concept of the cell. At any rate, his *Micrographia* served to stimulate other observers in the Royal Society, notably Nehemiah Grew, to prosecute his important studies upon vegetable histology and physiology. In the field of Astronomy, Hooke made a number of original observations pertaining to the orbits and behavior of several of the planets but for the most part he lacked the mathematical knowledge that would have enabled him to follow the clues through to their conclusion. Particularly was this true in connection with his views upon gravitation about which he had a rather acrimonious controversy with Sir Isaac Newton, in which he claimed priority of discovery.

His jealous and peevish temper frequently brought him into conflict with workers in the fields of science. Some of these controversies only embittered his opponents; others either halted the announcement of valuable discoveries or postponed them for so long a time that others obtained the credit for their discovery. In the case of the application of the spiral spring to watches, there was no question of Hooke's priority of discovery but owing to a disagreement about the terms of a patent which Boyle volunteered to procure for him, credit for the invention passed on to Huyghens in 1675, seventeen years after its discovery by Hooke. For certain of his venomous criticisms of Oldenham, the secretary of the Royal Society, he was taken to task and forced to recant. After Oldenham's death, however, he was chosen his successor which position he filled from 1677-1682, editing seven numbers of the philosophical transactions of the Society. In his later years, he continued his investigations and there was scarcely a single invention of his period that he did not make or claim as his own. He did actually make about one-half of the discoveries of his age. He designed an autocousticon, suggested a practical method of telegraphy, a universal joint, a sounding machine, the anchor escapement for clocks and many other mechanical devices. He also extended his interest into the fields of science, for he had ideas on the nature of fossil formation and the succession of living things upon the earth, which have been shown to be sound in the light of present-day knowledge. His last invention, a marine barometer, was described for him, before the Royal Society by Halley. This was in 1700. He was created a Doctor of Physic at Doctors Commons in 1691.

Always of insignificant stature, stooped in his carriage, even in youth, this attitude became a deformity in later years. Intensely active, quick-moving and restless, he burned himself out at about sixty-four years of age and his remaining three years were for the most part unproductive. The last year he became wholly blind. Death claimed him on the third of March, 1703. He lived an essentially monastic life, lacking in all the social virtues that human associations cultivate, an unlovable character. Even his genius suffered because of his estrangements from his fellows and much that he might have had the credit for, ultimately went elsewhere. Appraisal of the significance of the life of such a man is difficult. If the "capacity for taking infinite pains" is essential to the make-up of a genius, then Robert Hooke was not in that class. Probably mere versatility falls short of true genius. Some, however, of the mechanical devices he either invented or paved the way to the discovery of, were the first steps in Watt's and Stephenson's steam engines in the mechanical field, and the perfection of the microscope, the telescope and various meteorological instruments of precision, in the purely scientific fields. For these it is fitting that the part he played in advancing civilization should not be forgotten on this his Tercentenary.

The Massachusetts Medical Society

SECTION OF OBSTETRICS AND GYNECOLOGY*

C. J. Kickham, M.D., *Chairman*
524 Commonwealth Ave., Boston, Mass.

R. S. Titus, M.D., *Secretary*
472 Commonwealth Ave., Boston, Mass.

Gonorrheal Infection Complicating Pregnancy

Gonorrhea complicating pregnancy is not uncommon. Rapid invasion of the infection, before a developing pregnancy has blocked the uterine cavity, not infrequently results in termination of that pregnancy. Early miscarriage, therefore, in these cases is common. It very frequently happens that the etiological background is obscured by those symptoms referable to the miscarriage. Especially is this true of miscarriage followed by febrile reactions and acute pelvic symptoms. This latter represents, in a certain number of cases, the invasion of the pelvis by the gonococcus infection which follows rapidly the emptying of the uterus. In all miscarriage cases, and especially those occurring with the first pregnancy shortly after marriage, one should make a careful inspection of the meatus for clinical evidences of gonorrheal infection, and if there is any question, repeated smears from the urethra and cervix.

In pregnancy complicated by a gonococcus infection, treatment of the latter should be vigorously carried out, using the same technique, as would be used if the patient were not pregnant. One should employ the douches, suppositories, and local treatment, customarily used in these cases. A warm sitz bath, a cleansing douche, followed by a vaginal suppository containing two per cent mercurochrome, or one-half grain of methylene blue, with, if necessary, local applications to cervix and urethra of mercurochrome, is a dependable treatment. The knee-chest position after insertion of the suppository is an important detail.

A mercurochrome tablet against the cervix, retained by a dry wool tampon, with a small piece of mercurochrome tablet in the urethra, retained by a cotton pledget, is excellent office treatment in these cases.

At the end of the eighth month of pregnancy, treatment should cease, this because of the assumed theory that vaginal procedures prior to delivery increase the danger of puerperal sepsis. It has been repeatedly demonstrated that this active treatment during the first eight months of pregnancy will not cause miscarriage or premature delivery. Repeated smears should be taken throughout this period as a check on the progress of the treatment, and intercourse, naturally, is absolutely interdicted.

The management of the delivery of the patient with an active gonococcus infection raises two important points. First, special prophylactic measures for the baby's eyes, and secondly, the possibility of the infection of the obstetrician's eyes by a spatter of vaginal discharge during delivery. For the latter, glasses are a valuable protection and if any question of contamination arises, the immediate adoption of prophylactic treatment is most important.

In regard to the baby's eyes: the wise procedure in these cases is to institute active treatment, as if infection of the baby's eyes had actually occurred. It is wisest from all points of view, to delegate this care to an ophthalmologist. In the absence of the latter, the baby's eyes at birth should receive the usual prophylactic treatment and then at least twice daily for ten days, have the eyes washed out with boracic solution with the instillation of twenty-five per cent argyrol. The eyes should be carefully inspected twice daily and at the slightest suggestion of redness or discharge the ophthalmologist *must* be consulted. This active treatment in it-

*A series of short selected articles by members of the Section is being published weekly.
Comments and questions by subscribers are solicited and will be discussed by members of the Section.

self not infrequently produces a mild inflammatory reaction. With a beginning gonorrheal ophthalmia, the first smears are very apt to be negative, and no obstetrician is justified in assuming responsibility for what a given case may or may not be.

Symptoms resembling puerperal sepsis following, usually late, delivery of the woman infected with gonorrhea are frequently encountered, representing pelvic invasion following the removal of the obstructing pregnancy. The terminal manifestations of such an invasion are often abscess formation, primarily in a tube or tubes, but easily becoming the characteristic type of pelvic abscess. The ultimate pathology differs in this respect from the pus type in the nonpuerperal state which very uncommonly develops into a typical pelvic abscess.

A not uncommon complication of gonorrheal infection is abscess in Bartholin's gland. The usual management of these should be followed. Those which are allowed to rupture spontaneously have a very much higher percentage of permanent cures than those that are excised. Warm borax sitz baths, repeated several times daily, seem to hasten spontaneous rupture and to lessen the discomfort. Such an abscess may rupture during delivery. In cases observed there has been no noticeably increased post-delivery morbidity and lacerations have healed by first intention. The liberal use of antiseptics during the delivery of such a case is indicated.

Subsequent to the lying-in period the patient should be carefully investigated to determine if there is a persisting gonococcus infection which, if discovered, necessitates a continuation of active treatment.

It should also be remembered that a very considerable number of infections in women are acquired shortly after their recovery from childbirth. In these cases the irregular and excessively protracted flow is frequently attributed to delayed involution rather than to its real cause. Cases which describe too frequent "menstrual" periods within a few months postpartum should be viewed with definite suspicion until the possibility of a recently acquired infection is ruled out. The characteristic symptom of the invasion period of the disease, discharge, under these circumstances is of course very easily assumed to result from the usual childbirth injuries, the excessive flow to delayed involution, displacements, etc. The appearance of the urethra in these cases, is the most important single guide to a correct appraisal of the situation. A case with the above symptoms in the postpuerperal period, which has an inflammatory reaction in and about the meatus should be assumed to have a gonorrheal infection until the contrary is proved by innumerable smears.

THIRD ANNUAL POSTGRADUATE MEDICAL EXTENSION COURSE

The following sessions have been arranged by the Committee for the week beginning November 24:

Barnstable

Sunday, November 24, at 4:00 P.M., at the Cape Cod Hospital, Hyannis. Subject: Kidney and Bladder Diseases, A (Surgical): Hematuria: Its Significance in Surgical Diseases of Kidney and Bladder. Instructor: S. B. Kelley. J. I. B. Vail, Chairman.

Bristol South (Fall River Section)

Monday, November 25, at 4:00 P.M., at the Stevens Clinic of the Union Hospital, Fall River. Subject: Lung Collapse Therapy. Instructor: G. L. Stivers. Eugene A. McCarthy, Chairman.

Essex North

Friday, November 29, at 4:00 P.M., at the Hotel Bartlett, 95 Main Street, Haverhill. Subject: Accident Work in Cases Covered by Insurance. Practical and Professional Considerations. Instructors: Mr. Charles Horan and H. C. Marble. Francis W. Anthony, Chairman.

Essex South

Tuesday, November 26, at 4:00 P.M., in the Nurses' Home of the Salem Hospital, Salem. Subject: Kidney and Bladder Diseases, A (Medical). Acute Nephritis—Etiology, Diagnosis and Treatment. Nephrosis and Its Treatment. Instructor: L. H. Hoyt. Walter G. Phippen, Chairman.

Hampshire

Wednesday, November 27, at 4:15 P.M., in the Nurses' Home of the Cooley Dickinson Hospital, Northampton. Subject: Pediatrics: The Neonatal State and Its Diseases; Medical and Surgical Aspects. Instructors: L. W. Hill and H. W. Hudson, Jr. Robert B. Brigham, Chairman.

Middlesex South

Tuesday, November 26, at 4:15 P.M., at the Cambridge Hospital, Cambridge. Subject: Cancer of Stomach, Bowel and Genito-Urinary Tract. Modern Care of Inoperable and the Incurable; the Development of Improved Methods of Caring for These Cases with Less Pain and Discomfort with Minimum of Drug Therapy. Instructors: R. C. Graves and Horatio Rogers. Edmund H. Robbins, Chairman.

Norfolk South

Monday, November 25, at 8:30 P.M., at the Quincy City Hospital, Quincy. Subject: Arthritis: (a) Medical Care of Patient in the Home. (b) Orthopedic Treatment in Hospital and Aids in Home Treatment. Instructors: F. R. Ober and C. S. Keefer. David L. Belding, Chairman.

Plymouth

Tuesday, November 26, at 4:00 P.M., at the Brockton Hospital, Brockton. Subject: Kidney and Bladder Diseases, A (Medical): Acute Nephritis—Etiology, Diagnosis and Treatment. Nephrosis and Its Treatment. Instructor: J. M. Flynn. W. H. Pulsifer, Chairman.

Worcester North

Friday, November 29, at 4:30 P.M., at the Burbank Hospital, Fitchburg. Subject: Neurological Aids in the Diagnosis and Treatment of Disease from the Medical Viewpoint. Problems of History and Examination with Special Reference to (a) Neurosyphilis, Multiple Sclerosis and Other Degenerative Conditions. (b) Diseases with Acute Onset, such as Meningitis and Cerebral Accidents. Instructor: T. J. Putnam. Edward A. Adams, Chairman.

PHYSICAL THERAPY

The Committee on Physical Therapy of the Massachusetts Medical Society is prepared to assist any city or county medical society with advice and, in so far as is possible, to provide speakers for programs of medical meetings during the coming winter.

Talks, demonstrations, and motion pictures may be arranged in order to bring, to the general practitioner, practical suggestions as to the value and possibilities of physical therapy in the treatment of his patients. Many simple procedures of physical therapy which have proved of value should be more generally employed. These, as well as other methods, will be discussed. It seems to the Committee that the place which such measures may occupy in the treatment of many disorders might well be emphasized.

The following subjects are offered:

The Present Status of Physical Therapy.

Physical Therapy in General Practice.

Body Mechanics, Posture Training, and Therapeutic Exercise.

Massage—Indications and Effects.

Pathological Conditions Helped by Physical Therapy.

Phototherapy (Radiant Light and Heat).

Hydrotherapy.

Diathermy, Medical and Surgical, including Short-Wave.

The Committee is glad to welcome inquiries or requests.

FRANKLIN P. LOWRY, M.D.
GEORGE R. MINOT, M.D.
ROBERT B. OSGOOD, M.D.

MISCELLANY

AIR-CONDITIONED AMBULANCES

Air-conditioned ambulances, embodying the world's first commercial application of the new principle of controlled atmosphere for automobiles which is expected ultimately to become standard equipment on all passenger motor vehicles, are shortly to bring greater safety and comfort to New York's ill and injured.

Following an announcement before the Motor Bus Operators' convention in New Orleans that custom-made weather for motorists has reached the stage of engineering reality, Willis G. Gray made known recently that installation of the first of these motor-car air-conditioning units would be in one of the ten ultramodern "hospital rooms on wheels" which his concern operates in Manhattan, Brooklyn, the Bronx and London, England.

"Invalid transportation offers the most advantageous of fields for application of automotive air-conditioning," said Mr. Gray. "Invaluable medical advantages and practical comforts will accrue to the sick from controlled atmosphere in ambulances.

"They can be moved in a moderate temperature in summer and kept comfortable and uniformly warm in winter. They will breathe only the purest of purefied air, filtered and humidified or dehumidified. By keeping the windows closed at all times, the air will be kept constantly and completely clean within, even when it is dirtiest without, and all draft will be entirely eliminated.

THE USE OF PUBLIC FUNDS

A scathing denunciation of the proposed use of public funds by the PWA for a futile public health project was published in the November 1 issue of the *New York State Journal of Medicine*, the official organ of the Medical Society of the State of New York, which comprises among its membership 13,074 of the practitioners of the state.*

"The project," states the *Journal*, "calls for a survey of deaf children in Monroe County, New York, at a cost of $10,440. The prospectus states that Monroe County contains sixty of these children. Other evidence from the head of the Bureau for Handicapped Children in the New York State Education Department at Albany accounts for only fourteen such, exclusive of those already in the Averill Avenue Nursery. Hence, it is intended to spend $10,440 to survey these fourteen children."

The Medical Society of the County of Monroe, according to the *Journal*, has remonstrated against this step through its Public Health Committee, which reports that the plan has been studied by a sub-committee on Deafness and Hard of Hearing.

"Such a project," states the *Journal*, "has no health value whatever. It presupposes subsequent training of the deaf child for which no provision is made, and its value is emphatically questioned by educators. Since it is impossible to detect deaf children before the age of three years and, since the public and special schools take them over at five years of age, the whole project is limited to children between three and five years.

"The project is an unwarranted intrusion into a medical and educational problem by sponsors who

*Directory A. M. A. 1934.

are not certified as competent by either medical or educational authorities. In times of great depression, such as we are living through, it would hardly seem possible that funds could be wasted on so futile a project."—*Bulletin, Public Relations Bureau N. Y. State Medical Society.*

MASSACHUSETTS BOVINE TUBERCULOSIS

The Department of Agriculture has designated Massachusetts as a modified accredited area practically free from bovine tuberculosis. The total number of accredited states is thirty-one.

A CRISIS CONFRONTS NEW YORK CITY

Mr. S. W. Reyburn, chairman of the commerce and industry committee of the United Hospital Campaign Committee, affirms that a real crisis confronts New York City's 107 voluntary hospitals which are running into debt $4,500,000 annually. Several have already closed their doors and some have completely exhausted their funds. To meet the situation, a public appeal will be made for $2,500,000.

AIDS TO MASSACHUSETTS STUDENTS

More than $50,000 is being paid out to Massachusetts students each month by the National Youth Administration, according to statements by Mr. Arthur G. Rotch. The money distributed is for work and wages in a school.

Students in Middlesex College, Massachusetts College of Osteopathy, and the Boston College of Physicians and Surgeons have received small grants.

The three Class A Medical Schools were not included in the recently published list.

THE HEALTH SURVEY

On Friday, November 1, an important conference was held at the headquarters of the Massachusetts Medical Society at which Mrs. Miriam Steep, regional supervisor of the survey representing the Surgeon General of the Public Health Service, outlined the plan of procedure and informed the group that Miss Rose Flynn would be in charge of the project in Massachusetts and would have headquarters at 41 Pearl Street in Boston. Those attending the conference were Dr. Henry D. Chadwick, State Commissioner of Public Health; Dr. Charles E. Mongan, President of the Massachusetts Medical Society; Dr. A. S. Begg, Secretary, and Drs. Walter A. Lane, Ernest L. Hunt, Michael A. Tighe, Francis H. Dunbar of the Public Relations Committee, and Dr. Dwight O'Hara of the Committee on Public Health.

It was decided that the State Society would coöperate in every possible manner and that the officers of the District Societies, in which the studies are to be made, would be instructed to render all possible assistance. The nature of the investigation is such as to make it mandatory for the physicians of Massachusetts to give it their support if the results are to have any value. Mrs. Steep and Miss Flynn explained the method by which the enumerators would be trained and discussed in detail the schedule which is to be completed for each family study. They pointed out that these schedules are confidential and would not be made available for any purpose other than that of tabulation. Each schedule as completed by the investigator is to be cross checked in the local office and immediately sent to the headquarters in Detroit for tabulation. Matters which concern diagnosis are to be referred to the physicians who were in charge at the time the diagnosis was made. No diagnosis made by a nurse or lay person will be accepted. The entire program is to be carried out as a project under the Works Progress Administration and will provide work for a considerable number of the so-called white collar class.

General Plan of the Health Survey

A. Purpose — The United States Public Health Service coöperating with the state and city health departments is making a Health Survey and Study of Chronic Illness and Physical Impairments in the general population.

Information regarding the extent and severity of chronic diseases and physical impairments is meager and health authorities cannot prevent disease unless they know when, where and under what conditions it is occurring. The relative prevalence of various types of disease, the geographic location, the age, sex, occupation, and in particular the relation between disability and employment of persons affected will be studied. All this information is necessary before chronic diseases and disabilities can be prevented and controlled with the same degree of effectiveness as has been achieved during the past 50 years in the control of communicable diseases such as typhoid fever, smallpox, diphtheria, scarlet fever, etc.

Modern preventive medicine has increased the expectancy of life from about 40 years in 1870 to 60 years in 1935. But nearly all this good record has been due to the prevention and control of infectious diseases of childhood. It is now proposed to study the causes of chronic illnesses and disabilities which usually appear after middle age and which are so intimately associated with occupation and with the economic and social status and habits of the people. A careful analysis and study of the collected data will provide the Federal and State health authorities with information which it is hoped will serve as a basis for specific recommendations for the prevention and control of the chronic diseases.

B. Scope—The survey is to be carried on in 19 states, divided into 5 areas. Large cities, smaller cities and towns, and selected rural communities will be included*. A list of the states and cities which have been selected as bases of operations is included in Section 4. In the large cities, sample areas will be selected for enumeration. In smaller cities and towns, the survey will include all families.

*The centers of the five areas in Massachusetts are Boston, Fall River, Greenfield, Ipswich and Pittsfield.

Rural communities will be selected in areas where supervision and enumeration can be most satisfactorily arranged and where a representative sample of rural families can be interviewed.

The survey will include interviews with 750,000 families in about 95 cities and towns. An average personnel of 3500 will be engaged on the project with a peak employment of five to six thousand persons.

C. Duration—The survey will begin on October 15 and will require from four to five months for enumeration and editing in the field, and a somewhat longer period for coding, tabulation, and analysis. The field work will consist of the house-to-house canvass of a predetermined number of families in each city or community; careful editing of the schedules for completeness and consistency; a verification of diagnoses by doctors who attended the cases; and in some places transcription of records of hospitals, sick benefit associations, a survey of medical facilities, and probably, a survey of communicable diseases. The last four will be covered by special instructions later if they are included in the survey and become the responsibility of the present organization.

The field work for the Health Survey has been planned to end not later than March 15, 1936. It is hoped that in many cities, towns and rural areas it may be completed before that date.

The purpose of the Emergency Relief Appropriation is to provide the means for useful employment of persons who have been receiving relief. Therefore, the rules promulgated by the President and the Federal Works Progress Administrator require that nearly all of the persons employed on this project shall be taken from relief rolls. In order that the work may be conducted in an efficient manner provision is made for employment, in essential positions, of a few non-relief persons, whenever it is found that no competent persons are available from relief.

DRINKER RESPIRATOR PATENTS HELD INVALID

The District Court of Massachusetts has recently held invalid three patents numbered 1,834,580, 1,906,453 and 1,906,844, granted to Philip Drinker and Louis A. Shaw in an infringement suit brought against John H. Emerson by Warren E. Collins, Inc., manufacturers of hospital equipment in Boston, who were sole licensees under the patents. The defendant, John H. Emerson, maintains a machine shop in Cambridge for the manufacture of hospital and research equipment, and began the manufacture of respirators in 1931.

The patents covered the construction of apparatus for producing prolonged artificial respiration, especially for human beings suffering from infantile paralysis as well as in cases of gas poisoning, electric shock and drowning. These respirators worked admirably and have been in great demand for use in hospitals since 1929.

The court found that the defendant began to make his respirators after having seen the Drinker respirator. The defendant, however, excused his infringement on the ground that the patents were invalid because all the alleged novel features covered by the patents were old and disclosed in the prior literature.

After considering all the evidence and prior publications produced by the defendant the court agreed with the defendant that the Drinker patents were invalid. The important features of the patent claims of all three patents were found to be anticipated by prior publications, some as far back as 1876, or by prior issued patents.

The patent statutes permit the defendant in an infringement suit to excuse his acts if he can definitely prove that the patent or patents on which the suit is brought are invalid on account of prior knowledge, use or publication more than two years before the filing date of the patent application on which the patent was granted.—*Abstract from "Drinker respirator patents held invalid," by Joseph Rossman. Science 82: 221 (Sept. 6) 1935.*

THE WARREN TRIENNIAL PRIZE

The Warren Triennial Prize, of five hundred dollars, which was founded by the late J. Mason Warren, in memory of his father, and which is awarded every three years to the author of the dissertation considered most worthy of a premium, has been given by the General Executive Committee of the Massachusetts General Hospital to Dr. Norman E. Freeman, for his essay entitled "The Physiology of Gangrene." Honorable mention was given to Carl C. Speidel, Professor of Anatomy of the University of Virginia Medical School for his essay entitled "The Phenomena of Nerve Irritation and Recovery, Degeneration and Repair, as Revealed by Prolonged Observation of Individual Fibres in Living Frog Tadpoles." Previous to 1934 there have been sixteen awards of this prize, thirteen going to men in this country and three to foreigners.

SEDGWICK MEMORIAL MEDAL PRESENTED TO DR. HAVEN EMERSON

The American Public Health Association at its sixty-fourth annual meeting in Milwaukee awarded the Sedgwick Memorial Medal to Dr. Haven Emerson of the College of Physicians and Surgeons of Columbia University. The presentation was made by Dr. William H. Park, of the Department of Health of New York City. The medal was established in honor of the late William Thompson Sedgwick, of the Massachusetts Institute of Technology, and is awarded for distinguished service in public health.—*Science, October 18, 1935.*

COMPARISON OF DISEASE INCIDENCE IN CONNECTICUT WITH 1934 AND SEVEN YEAR AVERAGE

MONTH ENDING NOVEMBER 9, 1935

	1935					1934			
Diseases	Week ending Oct. 19	Week ending Oct. 26	Week ending Nov. 2	Week ending Nov. 9	Average cases reported for week corresponding to Nov. 9 for past seven years	Week ending Oct. 20	Week ending Oct. 27	Week ending Nov. 3	Week ending Nov. 10
Actinomycosis	—	—	—	1	—	—	—	—	—
Amebiasis	1	—	—	—	—	—	1	—	—
Chicken Pox	38	83	79	172	77	50	63	63	110
Conjunctivitis Infectious	—	—	2	—	—	—	—	—	—
Diphtheria	5	6	5	2	11	1	3	6	8
Dysentery Bacillary	3	—	—	—	2	—	60	5	—
Encephalitis Epidemic	—	—	1	—	—	2	—	—	—
Favus	1	—	—	—	—	—	—	—	—
German Measles	7	5	1	9	1	2	2	1	2
Influenza	2	—	9	1	2	1	1	2	2
Measles	38	58	66	32	36	46	51	72	145
Meningococcus Meningitis	—	—	—	—	1	—	—	—	—
Mumps	20	22	16	70	34	12	12	20	22
Paratyphoid Fever	—	—	—	3	—	—	—	—	—
Pneumonia (Broncho)	12	15	7	16	21	12	11	19	13
Pneumonia (Lobar)	12	18	12	15	21	11	9	18	19
Poliomyelitis	17	9	7	7	3	—	—	—	—
Scarlet Fever	24	44	30	32	41	24	25	31	37
Streptococcus Sore Throat	3	3	1	1	1	1	1	1	2
Trichinosis	1	—	3	—	—	—	—	—	—
Tuberculosis (Pul.)	22	17	28	24	24	24	19	34	25
Tuberculosis (O. F.)	—	—	2	2	2	—	1	1	2
Typhoid Fever	5	1	2	1	3	1	2	1	—
Undulant Fever	2	1	2	4	1	—	1	2	5
Whooping Cough	65	49	71	68	46	50	57	69	65
Gonorrhea	37	43	61	32	34	30	29	54	61
Syphilis	43	62	63	38	49	55	47	81	69

Remarks: No cases of Asiatic cholera, glanders, plague or yellow fever during the past seven years.

DR. AND MRS. WOJTASINSKI ARE FOUND GUILTY

Dr. Walter Wojtasinski and his wife, Katherine, of Ashmont street, Dorchester, trading as W. Wojtasinski Drug Company of Boston, manufacturers of "Katro-Lek," a patent medicine, were found guilty November 14, 1935, by a federal district court jury of mislabeling the product in violation of the Pure Food and Drugs Act.

The verdict was reached after the jurors had deliberated five hours. On recommendation of Charles A. Rome, assistant U. S. attorney, who prosecuted, the case was continued for sentence by Judge George C. Sweeney.

The government claimed that the circulars and packages had misrepresented falsely the curative and therapeutic remedies of "Katro-Lek."—*Boston Herald, November 15, 1935.*

FOOD AND DRUG FAKERS

The November 13, 1935 *Bulletin of the Department of Agriculture* gives details of more than twenty-five prosecutions with convictions for illicit trades in medicines and foods.

Manufacturers and sellers of medicines with fraudulent claims for the cure or relief of a great variety of diseases, have been fined in large amounts of over a thousand dollars in several instances.

These reports show remarkable success in controlling the distribution of alleged remedies and adulterated foods, for which the public is paying large sums of money.

Such expenditures are wasted and in most cases of drugs more than wasted, for in many cases the resort to such preparations leads to neglect of effective treatments.

CORRESPONDENCE

SUPRARENAL CORTEX EXTRACT IN THE TREATMENT OF VOMITING IN PREGNANCY

Worcester State Hospital
Worcester, Mass.

November 6, 1935.

Editor, *New England Journal of Medicine*,

In the issue of the *Journal* of Volume 213, p. 885 of the week of October 31, the article under the Section of Obstetrics and Gynecology outlining treatment in the cases of vomiting in pregnancy has not taken into account one of the latest methods of therapy which seems to be very beneficial. This treatment consists of intramuscular injections of suprarenal cortex extract.

The articles of Kemp in *Endocrinology* (16: 434, 1932), and in the *Canadian Medical Association Journal* (28: 389, 1933), also Freeman and Melick in the *American Journal of Obstetrics and Gynecology* (29: 602, 1935) would indicate that this treatment has proved effective when other methods have failed. The rationale behind the treatment would appear to be the substitution of an active principle of the suprarenal gland which shows a relative deficiency during pregnancy. It could be postulated that in these cases the hypertrophy of the adrenal gland, which is prone to occur in normal pregnancy, has not been sufficient to take care of the extra load on the mother and for this reason relative deficiency in cortical hormone occurs. This leads to nausea and vomiting of the same type as is found occurring in Addison's disease. The giving of small amounts of suprarenal cortical extract appears to be specific therapy for this condition.

Very sincerely yours,

JOSEPH M. LOONEY, M.D.,
Director of Laboratories.

IODINE AS AN ANTISEPTIC

Mallory Institute of Pathology
Boston City Hospital
Boston, Mass.

Editor, *New England Journal of Medicine*,

The letter from Dr. Elliott C. Cutler in the November 7th issue of the *Journal*, relative to the recent editorial on "Iodine as an Antiseptic," is deserving of comment. Dr. Cutler admits the *in vitro* germicidal efficiency of iodine, but questions its value as an antiseptic, particularly in relation to skin disinfection. It should be noted that no reference to skin disinfection was made in the editorial. Furthermore, the solutions referred to were all aqueous and one would not expect such to be used on the skin, unless the latter had been prepared in some way so that these aqueous solutions could penetrate the hair follicles and sweat glands. Be that as it may, the writer feels that little, if any, experimental evidence has been submitted which has proved iodine to be less effective than any other antiseptic, regardless of how or where it is used. Even those authors referred to in Dr. Cutler's letter, who might be considered the most impartial, came to the conclusions which are at variance with what he maintains. Simmons (U. S. Army Medical School) concluded, in part, in his 1928 article that " . . .from the standpoint of bactericidal action, tincture of iodine (U.S.P.) was found to be far superior to any of the solutions when used on the unbroken skin . . ." and in his 1933 article that " . . . mercurochrome . . . should not be considered as a substitute for iodine"; and Smith (Medical Corps, U. S. Army) concluded, in part, that iodine is "an excellent skin disinfectant".

The majority of recent articles on antiseptics reveal the marvelous bactericidal and bacteriostatic properties of certain mercurial compounds and it is the latter—the bacteriostatic or growth inhibiting property—which has led to many conclusions which, to the writer, are false. Shippen was the first to draw attention to the fact that in the standard *in vitro* bactericidal tests sufficient amounts of mercurial compounds may be contained in the single loopful of the antiseptic-culture test mixture to inhibit growth in the culture tube. For this reason, he recommended that a second transfer be made from the first culture tube to a second. A specific example may be taken from experiments conducted in this laboratory. In tests using the "F.D.A. method (special) *S. aureus*, 37°C," certain mercurial compounds did not show growth in the first culture, but did in the second, of transfers from test mixtures ranging in concentration of the antiseptic from that recommended for use to a dilution of 1:32. As the test mixture contained 5.0 cc. of antiseptic plus 0.5 cc. culture, the transfer (1 loopful) 0.02 cc. and the culture 10.0 cc., this means that a usable solution

concentration of $\frac{1}{32} \times \frac{5}{5.5} \times \frac{1}{50} \times \frac{1}{10} = \frac{1}{17600}$ is sufficient to inhibit the growth of the staphylococci, even though the undiluted antiseptic is unable to kill the bacteria under the conditions of the experiment. In skin scraping and biopsy tests, such as those cited by Dr. Cutler, mercurial compounds have shown up exceptionally well, but no suitable controls, comparable to the Shippen modification, can be made for bacteriostatic concentrations. The antiseptic and bacteria are intimately connected with the material and, unless cultures have been applied to the skin, effective bacteriostatic dilutions are undoubtedly much higher, due to the relative scarcity of bacteria.

It is acknowledged that the bactericidal effect of iodine is diminished by the presence of serum, but the writer has failed to find any mercurial antiseptic which, in the recommended usable concentration combined with an equal amount of horse serum, will kill *Staphylococcus aureus* in five minutes. On the other hand, a 1:32 dilution of Lugol's Solution, U.S.P., will kill under identical conditions. Some mercurial compounds, mercury oxycyanide (1:4000), mercurochrome (1:50), merthiolate (1:1000) and

merphenyl nitrate (1:1500), will not kill in these usable concentrations, even in the absence of serum.

As Dr. Cutler has stated, "the true appraisal of an antiseptic is a difficult measure". Numerous properties have to be taken into consideration and many claims have to be disproved. So much trash has appeared in the advertisements of commercial antiseptics within recent years, that an attempt at an impartial evaluation has been undertaken in this laboratory. Although the work has not been completed, everything to date points to iodine as the most efficient *wound* antiseptic. If equitable and comparable tests can be devised for testing skin disinfectants, the writer feels that iodine will again emerge on top.

Very truly yours,

ROBERT N. NYE, M.D.

PNEUMONIA DEATH RATE

The Commonwealth of Massachusetts
Department of Public Health
State House, Boston
November 6, 1935.

Editor, *New England Journal of Medicine*,

On October 26, 1935, *The Boston Herald* printed a dispatch from New York to the effect that the death rate in pneumonia can be reduced by 50 per cent by the use of newly developed serums. In part this is true, but the statement needs qualifying. About three-quarters of all pneumonias appear due to pneumococci. These organisms, however, are not all alike and by immunological methods can be separated into distinct types, at least thirty-two of which have been recognized in this and other countries. There are serums available to combat pneumonias due to some but not all of these types. Satisfactory serums have not been produced for the treatment of cases caused by other organisms.

The early use of potent serum has been shown to reduce the death rate of pneumonias caused by Type I pneumococcus by over 60 per cent and in Type II cases by nearly 50 per cent. Pneumococci of these two types are of the greatest importance and are responsible for about one-quarter of all cases of pneumonia. Serums used to treat such cases can scarcely be called "newly developed" as they have been in use since 1910. Within the past six to eight years serums have been prepared against several of the other types of pneumococci. They have been somewhat extensively used in New York City and good results are claimed from the treatment of pneumonias caused by these types—such as Types VII and VIII and a few others. Sufficient cases treated with and without such serums have not yet been obtained to establish their value clearly. Nevertheless, the results appear very encouraging.

The usual death rate of Type I cases not given serum is about 25 per cent. This can be reduced to 10 per cent if serum treatment is begun within the first four days of illness, and to 7 per cent when such treatment is begun within three days of the onset. Similarly in Type II cases the usual death rate of 40 per cent can be reduced to 25 per cent or less by early treatment.

A study of pneumonia death rates brings to light the interesting fact that nearly two-thirds of pneumonia deaths occur in males. Excess death rates for males from birth to puberty and from twenty to sixty years of age have been found. This is especially true in the latter age group in the most highly industrialized communities and tends to disappear in rural areas. Further, in the United States, pneumonia appears far more prevalent along the Atlantic seaboard from Maine to Georgia (inclusive) and in a group of Southwestern states encompassing the Colorado Plateau than elsewhere.

A study of the ten original registration states and of Massachusetts death rates from pneumonia indicates that only a slight downward trend has occurred during the past thirty-five years. Thus pneumonia as a cause of death is but little less common than formerly.

Very truly yours,

RODERICK HEFFRON, M.D.,
In Charge of the State Department
of Health Pneumonia Study.

DR. CHARLES H. MAYO EXPLAINS CERTAIN QUOTED STATEMENTS IN NEWSPAPERS

Editor, *New England Journal of Medicine*,

The following is an account of what happened at the meeting of the Inter-State Post Graduate Medical Association of North America in Detroit and a digest of my words and thoughts:

I had my manuscript with me but spoke without it. My main subject was "Goiter and the Changes in Its Treatment." I recalled the cretins whom I saw several years ago in Switzerland when visiting Dr. de Quervain. Cretins are seldom seen now because of recognition of the disease and administration of thyroid, either to the patient or to the expectant mother; also by administration of thyroid to myxedematous persons, they can be rendered mentally active. When the thyroid is overactive, as it is in exophthalmic goiter, there is a markedly increased metabolism. These varied states are due to deficiency or increase of thyroid secretion with secondary effect on the capillary circulation of the body including, one would expect, that of the brain.

Reduction in the circulation, not always continuous, might conceivably bring on mental changes in conditions in which the thyroid was not involved. These changes may go on for varying periods in the early stages, but eventually become permanent and close, in part, the function of the brain. Vascular constriction, when it occurs in other parts of the body than the head, as it does in Raynaud's disease, is not necessarily permanent in the early stages. Emotional disturbances are known to be potent in the crises both of Raynaud's disease and psychic disorders. This similarity in the course of the vascular condition and of certain psychic conditions

tends to suggest that the vascular constriction may be a factor in the psychic abnormality.

There is experimental evidence that control of the circulation of the brain can be exerted through the carotid bulb, but it cannot be denied that to prove an effect on the circulation of the brain is difficult, because the vessels of the brain are relatively inaccessible. Nevertheless, the head is an extremity of the body, just as are the hands, and it is well known that when the blood vessels of the hands are not obliterated but are constricted, as they are in Raynaud's disease, they can be made to dilate by local anesthesia, general anesthesia, or induced fever, and that permanent dilation can be brought about by the operation known as cervicothoracic sympathectomy. Also, a temporary good effect has been produced in certain forms of insanity by applying, to the head, methods similar to those that have been applied to the other extremities. There seems nothing unreasonable in the assumption that the cause of the observable effect on the mental condition in early cases might be the same as the cause of the observable effect on the hand or the foot, if the arterial condition of the brain in certain types of insanity is analogous to the arterial condition of the hands and feet in Raynaud's disease. At all events, the treatment has been tried, notably in the catatonic form of dementia praecox.

I do not think that the physicians before whom I spoke were for the most part startled by what I said for they heard the context and my inflections and thus were in a position to sketch in a background which I thought I implied but knew that I had not time to delineate. I said that the effects of the treatment had worn off in three weeks, but I voiced the hope that methods of injection or operation would be found to make them permanent in treatment of patients who had not been mentally affected for too long a time. I spoke to stimulate others to seek methods of controlling the circulation of the brain, such as have been found to control the circulation of other extremities. I estimated that at least five years would pass before such methods would be found.

If my expression of a hope inadvertently took the form of a prophecy it would not be strange, for, in more than fifty years of the practice of medicine, I have seen very many times when the general opinion was that all that would ever be known or done in a certain field already was known or had been done. I never believed this in any instance and I have not been disappointed in my hope that in any field concerning which science has a hint, ultimately more would be known.

However, the effects in the forms of insanity which I referred to have been only temporary, and not I, my colleagues, nor any others of whom I know, are yet prepared to effect a cure.

Sincerely yours,

CHARLES H. MAYO,
Rochester, Minn.

November 9, 1935.

RECENT DEATHS

BLANCHETTE—ALEXANDER BLANCHETTE, M.D., of Haverhill, Massachusetts, died in that city, November 13, 1935, by suffocation due to a fire.

Dr. Blanchette was born in 1869 and graduated from the University of Bishop College Faculty of Medicine, Montreal, Canada, in 1892.

GOODWIN—EDWARD EVERETT GOODWIN, M.D., of 436 Elm Street, Brockton, Massachusetts, died in the Emerson Hospital, Boston, November 6, 1935.

He was born in North Mariaville, Maine, October 28, 1864, the son of Mr. and Mrs. George P. Goodwin.

After his early education in Maine public schools he studied in Dedham and Brockton schools, later attending Boston University School of Medicine, graduating therefrom in 1899.

He was a Fellow of the Massachusetts Medical Society and the American Medical Association. In addition to his professional activities he was prominent in religious and civic organizations including the Massachusetts Homeopathic Society, the American Institute of Homeopathy, the Boston Surgical Society, the Brockton Medical Society, Paul Revere Lodge, Free and Accepted Masons, Satucket Chapter, Royal Arch Masons; Brockton Council, Royal and Select Masters; Bay State Commandery, Knights Templars; Massachusetts Consistory and Aleppo Temple, Ancient Arabic Order of Nobles of the Mystic Shrine.

He is survived by his widow, Mrs. Myrtle E. (Hollis) Goodwin; two daughters, a brother, and two sisters.

OBITUARY

DR. LEONARD WHEELER*

Leonard Wheeler, M.D., for sixty-five years a member of the Massachusetts Medical Society and from 1872 to 1912 a practicing physician in Worcester, died at his home there October 2, 1935, aged ninety years and thirty-two days.

Born in Lincoln, where his emigrant ancestor settled in 1642, he prepared for college at Phillips Exeter Academy, joined the sophomore class at Harvard in 1863, graduated in 1866 and in 1870 received his M.D. degree, after three years at the Harvard Medical School and one as medical interne at the Massachusetts General Hospital. The next two years he spent in medical studies in Breslau, Leipsic and Vienna, coming in close contact in the latter city with such men as Rokitansky, Freund and Schroeder. In 1872 he came to Worcester as Superintendent of the Worcester City Hospital, organized the previous year. This hospital, at that time the only one in the city, had but eight beds and the Superintendent was allowed, in addition to his duties there, to attend to private patients at their homes.

*Presented to the Worcester District Medical Society by the committee duly appointed.

As a general practitioner giving special attention to obstetrics and operative gynecology, Dr. Wheeler ranked for forty years among the leaders of the profession in the city and county. In 1874 he resigned his superintendency but retained his connection with the hospital until his death sixty-three years later, serving as visiting physician until 1888, as obstetrician from that time until 1896, and for the remainder of his life as consulting obstetrician and a member of the general consulting staff.

Soon after he came to Worcester, the Washburn Free Dispensary was opened and from 1875 to the time of his death he was connected with that institution with the Memorial Hospital of which the Dispensary became the Out-Patient Department when the hospital opened its doors in 1888. He served on the hospital staff as physician and surgeon until 1900, when he became a Trustee, was President of the Board from 1904 to 1917 and Vice-President from 1917-1925.

He was a member of the Consulting Staff of St. Vincent Hospital for twenty-five years, was a Trustee of the Foxboro Hospital 1905-07, Secretary of the Worcester District Medical Society 1873-75, Vice-President 1893-95, President 1895-97 and Vice-President of the Massachusetts Medical Society 1906-07.

A charter member of the St. Wulstan Society, of the Worcester Club and of the Tatnuck Country Club, he was also a member of the American Antiquarian Society, the Worcester Fire Society, the Worcester Art Museum, of various other civic organizations and of the Harvard Club of Worcester and the Union Club of Boston.

In 1881 he became a Corporator of the Worcester County Institution for Savings, a Trustee in 1889, and for the last thirteen years of his life served as one of its three Vice-Presidents.

A discriminating student of history, a writer of numerous medical articles, the Librarian for many years of the local Medical Society's library, it was always a pleasure and a privilege to listen to his opinions on medical, social and historical matters.

Handicapped for many years by various physical disabilities, he retained to the very end of his life a keenness of mind that was a delight to everyone that knew him. There was no observable failure of his mentality and no one who came in contact with him could have suspected that but one member of the Massachusetts Medical Society, Dr. Stevens of Cambridge, had been a member longer than he.

Dr. Wheeler married Elizabeth Bancroft Cheever, daughter of the Rev. Henry Cheever, November 29, 1897.

He is survived by his widow, four children and three grandchildren. His son, Bancroft C. Wheeler, is at present an Assistant Surgeon at the Memorial Hospital.

SAMUEL WOODWARD,
HOMER GAGE,
DAVID HARROWER.

NOTICES

THE APPOINTMENT OF DR. R. H. GUTHRIE

RILEY H. GUTHRIE, M.D., has been appointed Chief Executive Officer of the Boston Psychopathic Hospital.

A COURSE BY PROFESSOR GEORGES PORTMANN

Professor Georges Portmann will conduct an intensive five weeks' course in Oto Rhino Laryngology in the University of Bordeaux, France, beginning July 30, 1936. English language, didactic laboratory clinical and operative instruction.

For particulars address Dr. James A. Flynn, 1511 Rhode Island Avenue, N. W., Washington, D. C.

BOSTON UNIVERSITY SCHOOL OF MEDICINE SURGICAL CLINIC AT THE BOSTON CITY HOSPITAL

Friday, November 22, 12-1, Cheever amphitheatre.

Dr. Frederic J. Cotton will speak on "Fractures of the Wrist and Ankle."

Physicians and medical students are invited.

REPORTS AND NOTICES OF MEETINGS

TESTIMONIAL EXERCISES FOR DR. EDSALL

Dr. David L. Edsall, recently retired dean of the Harvard Medical School and School of Public Health, was honored with a testimonial meeting and dinner held by the Harvard Alumni Association Wednesday, October 23. The afternoon meeting was held at the medical school with Dr. Walter B. Cannon presiding. Dr. Cannon, in reviewing Dr. Edsall's contributions to the medical world in the past twenty-five years, emphasized his investigations in occupational disease, and the impetus which he early gave to the study of this relatively new branch of medicine. His efforts in the advancement of the Harvard School have been unequaled except by those of Dr. Eliot.

Three addresses were delivered on the subject, "The Development of Medical Education in the United States Since the World War." Dr. Walter A. Jessup, President of the Carnegie Foundation for the Advancement of Teaching, was the first speaker in this group. In tracing the evolution of medical teaching from ancient times, he told of man's constant struggle against disease, and his steady search for aid in scientific and pseudoscientific fields. Many forces have hindered the study of medicine. Ignorance and superstition long prohibited dissection and the study of gross anatomy. Absolute acceptance of the authority of Hippocrates and Galen hindered advance for centuries. The academic teaching of medicine with law and theology provided little stimulus for experimentation and advancement of medical knowledge. Then for many years the study of medicine became an apprenticeship, with medical schools serving only as centers for academic lec-

tures. Little or no coördination existed with other branches of the university, if indeed the medical school was connected with a university at all.

Early in this century the American Medical Association sought the aid of the Carnegie Institute for the Advancement of Teaching in an attempt to improve the quality of medical instruction. This committee, headed by Dr. Flexner, emphasized the necessity of thorough scientific instruction of medical students before clinical exercises were undertaken. As a result of this report many inadequate medical schools have been closed since 1910, and the character of those remaining has been greatly strengthened with the development of strong preclinical departments. An indirect result of this development has been the domination of medical thought by great scientific institutes for research. The application of scientific methods to the solution of public health problems has brought about the practical elimination of certain diseases such for example as typhoid fever, and yellow fever. Large corporations have realized the value of, and have aided in the application of public health measures to industry, with the resultant elimination of many occupational diseases.

Dr. Edsall emphasized the importance of personality and human kindness to the physician. He advocated a thorough knowledge of literature, believing that such knowledge was essential for an understanding of human nature and a correct evaluation of laboratory data. Within recent years great strides have been made in the cultural education of students before they enter on a purely medical course.

Under Dean Edsall, Harvard was anxious to meet the demands for education in public health. He established the requirements of a scientific background to such an education, as well as a thorough knowledge of adjoining fields such as sociology and psychology.

Harvard Medical School, one of the most richly endowed schools in the world, has well met her obligation to society. No small part of her success is due to the efforts of Dr. Edsall.

Dr. Eugene DuBois, Professor of Medicine at Cornell Medical College, talked of the influence of the preclinical sciences on clinical medicine. A generation ago the aim of medical schools was to prepare their students to secure interneships. No effort was made to stimulate reading of original articles, and teaching was done entirely from textbooks. Dr. Edsall changed the whole atmosphere of medical education. He favored the elimination of the "spoon feeding" system, and advocated the wider use of source material instead of textbooks. He introduced the tutorial system which allowed more leniency to exceptional students, with the opportunity for special work in selected fields.

The division between preclinical and clinical subjects has been overemphasized. The teaching of the preclinical courses in conjunction with other college courses, as is done in some schools, is not desirable. They should be more closely welded to the clinical departments of the school, at the expense of some separation from the rest of the college courses if necessary.

In recent years the additions made by clinical investigators to scientific knowledge have increased tremendously. The narrow concept that "work on animals is more scientific than work on man" is no longer tenable. Many of the modern reviews on physiology and biochemistry are largely referable to clinical work.

The organization of the present-day clinic is open to many criticisms. Some need complete reorganization. Financial depression has limited the funds available for research, which forms an important part of every modern clinic. Young men interested mainly in caring for patients or teaching feel that they must do a certain minimum of research if they are to gain academic advancement. Those interested mainly in research see a future only as assistants if they remain in laboratory work alone. With academic advancement and increase in administrative duties, there is a steady decrease in the extent of researches performed by men formerly very active, and often the appointment to a professorship entirely curtails further investigative work.

A new type of organization is suggested which will take advantage of clinical material, but with appropriations separate from those of the hospital housing it. Its board of directors and connections should be such as to allow the staff to move from one hospital to another to obtain the clinical material needed for the problems under consideration at any one time. Administrative duties should leave the staff adequate time for investigative work. Such a system would improve the character of medical instruction, and while decreasing the quantity of research published would definitely improve its quality.

Dr. Lawrence J. Henderson, Professor of Chemistry at Harvard, in delivering the closing address of the afternoon spoke of the various interactions between medical and other sciences. In early times the path to other fields lay through medicine, and many of the concepts of other branches of knowledge were made by men who began their careers as physicians. Then came the period in which contributions to medical knowledge were largely made by workers in other scientific fields. This period is exemplified by the contributions made by Lavoisier, a chemist, to the study of metabolism, and the fundamental concepts given by the chemist Pasteur to the field of bacteriology.

A generation ago chemistry, physics and other "pure sciences" were still quite independent of medicine. The frontiers of science were then several and real. Now these several frontiers have become false and unreal. Medicine and the various sciences can no longer be clearly demarcated, and segregated. Advancement in one field usually influences all the rest.

At the time Dr. Edsall began his deanship, the

"Guild Economy" was in full swing. The medical school was isolated from the rest of the university and the laboratories were segregated from the clinics. These isolations were intellectual as well as physical. Dr. Edsall had experienced the detrimental influence of this system in his early experimental clinical studies, and in the application of clinical methods to industrial hygiene. He undertook to eliminate this "pigeon hole" method of investigation and teaching. In the founding of the School of Public Health, intimate relationships were established with the Medical School. The close relationships now existent between the school and the Children's Hospital, the Fatigue Laboratory, and the Engineering School are examples of the success of his efforts to abolish the "Guild System". He had a large part to do with the founding of the Committee on Industrial Hygiene, which administers large grants from the Rockefeller foundation. This committee has given funds to such apparently diverse enterprises as the Harvard Expedition to Chile, the Fatigue Laboratory, and the department of anthropology. An example of the interrelationships of the various sciences which have been promoted is afforded by the presence of a physicist on the Cancer Commission, and a mathematical statistician on the faculty of the School of Public Health.

The institution of the tutorial system at Harvard has greatly aided undergraduates in shaping their studies. The presence of young medical men among the college tutors has promoted and inspired a better relationship between the medical and college faculties.

In all these advances toward closer collaboration Dr. Edsall has taken a leading part, and it is chiefly through his efforts that many of the results have been achieved.

The testimonial dinner was held at the Harvard Club with Dr. Conant presiding. Dr. Conant expressed his appreciation of the encouragement, cooperation and assistance which Dr. Edsall had so freely given him since his appointment as president of the university. Dr. C. Sidney Burwell, new dean of the medical school, spoke briefly of Dr. Edsall's contributions to pediatrics, occupational disease, public health, and the advancement of Harvard Medical School. The change from academic to bedside teaching, the development of a well functioning tutorial system, and the encouragement given to research contributed much toward keeping the Harvard Medical School among the leaders of present-day medical education.

Dr. A. Lawrence Lowell, President Emeritus of Harvard University, emphasized Dr. Edsall's advancement of the Medical School by the union promoted between the preclinical and clinical sciences, and the harmonious relationships developed between the various departments. The value of a general examination over the whole of the four-year medical course was recognized by Dr. Edsall, and he succeeded in establishing it a year after assuming his office as dean. His introduction of the system of "self education" instead of the academic teaching of "pre-digested" information has been one of the greatest contributions to modern medical instruction.

The address of Dr. Edsall will be printed in its entirety in a future issue of this Journal.

HARVARD MEDICAL SOCIETY

The Harvard Medical Society held its first meeting of the current year at the Peter Bent Brigham Hospital, October 22, Dr. Henry A. Christian presiding.

Two cases were presented; the first, a medical case, by Dr. Sullivan.

A thirty-seven year old Canadian male entered the hospital five days previously, with the history of persistent vomiting for the past three weeks. He had been under medical treatment for peptic ulcer fourteen and ten years previously, but since that time had been well until the onset of the vomiting.

Physical examination revealed him to be markedly dehydrated and cyanotic. There were râles at both apices, and tenderness in the right upper and lower quadrants.

Laboratory studies: urine, very slight trace of albumin; specific gravity varying from 1.010 to 1.014. P. S. P. test of renal function showed excretion of but 30 per cent of the dye in three hours. Blood: red cells 5,400,000, hemoglobin 123 per cent, white count 15,000.

He was placed under routine ulcer management with frequent feedings and alkali powders, but vomiting persisted for the four days. On the fourth day there was marked increase in the cyanosis, and the patient complained of headache. Chvostek's and Trousseau's signs were present. The blood carbondioxide combining power was found to be 108 volumes per cent. He was given ten grams of ammonium chloride in one hundred cc. of normal sodium chloride solution by rectum. He became lethargic and semicomatose on the morning of the fifth day, when his blood urea nitrogen was 159 mgs. per cent. Forty-five hundred cc. of normal saline solution was then administered subcutaneously and intravenously with subjective improvement, disappearance of lethargy, and disappearance of Trousseau's and Chvostek's signs. The carbondioxide combining power of the blood fell to 86 volumes per cent and the blood sodium chloride rose from 235 milligrams per cent, the next morning, to 300 at three P.M., and the serum calcium was 7.4 mg. per cent, the serum phosphorus 11 mg. per cent. Dr. Aub, in discussing the case, emphasized the great constancy of the blood base, and the fact that other substances were retained or excreted to maintain it as constant as possible. In this case salt was lost in the vomitus, and there had been inadequate elimination of bicarbonate in the urine. There was a decrease in the available calcium ions, and tetany developed. High values of blood base result in damage to the kidney with rise of the blood urea nitrogen, due to retention.

Dr. Emery commented on the frequent upsets experienced by patients on the Sippy diet with high alkali intake. Ill effects are more apt to occur in patients with previously damaged kidneys, although they may occur in those with normal kidneys. Change from calcium to bismuth compounds will relieve the toxic symptoms in many cases, even though the proportion of soda administered remains the same.

Dr. Christian stated that either alkalis or acids in large excess above normal will produce a toxic nephritis, experimentally. The development of evidence of alkalosis in ulcer patients should always lead one to expect renal impairment, since the normal kidney is capable of excreting excessively large amounts of bases or acids. Headache is a very early symptom of renal dysfunction in patients on ulcer treatment.

The second case was presented by Dr. Ryder: A seventy-three year old white male entered with a history of typical angina pectoris for the past ten years. For the past two years he had suffered attacks of upper abdominal pain distinct from his anginal attacks, and characteristic of gall bladder disease. Four months ago he had severe right upper quadrant pain radiating to the angle of the right scapula, associated with nausea, vomiting, and jaundice (icteric index: 40.) X-ray studies revealed a pathological gall bladder. He was sent home because he was considered a poor operative risk. Thirty-six hours before his present entry he suffered abrupt onset of diffuse upper abdominal pain, worst in the epigastrium, and not relieved by nitrites.

On entry his white count was 14,000, temperature 101°, and his urine showed a 1 plus test for bile. The icteric index was 12.

Dr. Cutler expressed the opinion that cholecystectomy was not justified in this case because of his poor condition.

Dr. Cheever stated that in his experience, patients suffering from both angina pectoris and gall bladder disease often receive considerable relief of their angina after cholecystectomy. A possible explanation of this phenomenon might be the abolition of reflex nervous or infectious stimulus to the heart. The evidence of gall bladder infection with the last attack points to the likelihood of more trouble in the future. He advised operation.

Dr. Christian concurred with Dr. Cheever. In his experience patients with combined angina and gall bladder disease stood cholecystectomy well and were often relieved of symptoms of both diseases postoperatively.

Dr. Walter B. Cannon, George Higginson Professor of Physiology, at Harvard Medical School, then recounted in delightful fashion some of the interesting features and impressions of his recent trip to the Orient, Russia, and Scandinavia.

He was very favorably impressed with the efforts for advancement of public health in China, which are under the able direction of Dr. J. Heng Liu, a graduate of Harvard Medical School. Recently a new medical school has been founded in Nanking with the specific purpose of developing men for service in the Public Health Department.

In Russia, Dr. Cannon was impressed by the regard paid to the human factor in labor, and by the facilities provided by the Government for the recreation of the working class. An earnest attempt is apparently being made to utilize, profitably, the leisure afforded by the thirty-hour working week. Large, beautifully landscaped "parks of culture and rest", provided with reading rooms, outdoor theaters, children's nurseries, game rooms, etc., are to be found in the large cities. An effort to popularize education and appreciation of art is also quite noticeable, although such effort is always colored with propaganda. Young men of promise are now being encouraged to enter the field of medicine by the expedient of doubling the salary paid to physicians by the state; huge institutes for research have been built, and great activity in scientific fields is in progress.

The increase in patients suffering from neuroses has been quite marked in Russia during the last decade. A quite probable explanation of this increase lies in the demands of time and machinery on a previously leisurely, rather primitive agricultural people, and also in the operation of fear.

In marked contrast to Russia were the Scandinavian countries with their fine educational systems, and great coöperative programs. To Dr. Cannon these seemed the most civilized countries in the world.

WILLIAM HARVEY SOCIETY

The first meeting of the year of the William Harvey Society was held on October 25 in the Beth Israel Hospital. Dr. Walter C. Alvarez spoke on "Functional Digestive Disorders." He was introduced briefly by Dr. Louis F. Curran.

In Doctor Alvarez's practice he finds that fully one-third of his patients show no evidence of organic disease and he believes that medical schools do not, as a rule, give adequate training to their students who will later have to meet functional problems almost as often as organic. A detailed history, taken with great care, should reveal the diagnosis of functional trouble even before the physical examination and laboratory work are done. It frequently requires several visits with the patient before the real truth becomes evident, since the idea of a functional disorder is most distasteful to the average person, who wants an operation and a rapid cure. Extreme care is needed in creating the proper frame of mind in such patients if one is to bring about restoration to health. It must be pointed out that many under the strain of certain unfortunate circumstances become neurotic.

Of course it is always necessary to make a most careful examination of all patients regardless of whether the disease is organic, because frequent

mistakes will otherwise be made and because there is nothing so convincing to a patient as a thorough physical examination.

A patient with organic disease is always straightforward and direct in his answers to the doctor's questions, while the neurotic individual dodges and refuses to "stick to the point". Dr. Alvarez spoke particularly of what he chose to call the "constitutionally inadequate" patient. Such people are often intellectually alert but seem unable to meet the strain of everyday life. The doctor cannot cure this type of individual, but he can often guide him into some occupation where he will be able to meet the requirements adequately, pointing out that there are limitations to every man's ability.

Doctor Alvarez's lecture was replete with excellent examples through which he drove his points home. He particularly stressed the necessity of a careful history and said that frequently when one doctor fails to get at the underlying cause of a functional disorder, it is wise to let another physician try to discover an etiology. It is important to find out the precise circumstances under which the difficulty began. It is rare to have functional attacks at night. Note the type of pain and have the patient point out exactly where it is, for a neurotic often complains of burning pains and is indefinite when asked to put his finger on the exact site. Functional pain is usually unrelated to any of the functions of the body and is unrelieved by certain measures that usually help organic digestive disturbances, as for instance the Sippy régime in gastric or duodenal ulcer. Pain due to migraine always follows a headache. The general sensitivity of the patient should be noted. Those patients that cry out repeatedly during a barium enema and have much pain at the dentist's are probably abnormally sensitive to all pain.

The family history often makes a diagnosis, for many of the constitutionally inadequate may be mildly insane and give a family history of insanity. In treating these patients, sympathy is most important and a brutal heartless approach will only drive them elsewhere. Insomnia is a frequent complaint and must be combated. Barbiturates may be used, because rest, often in the daytime but certainly at night, is essential. Doctor Alvarez often uses some active treatment because it gains the patient's confidence and gets him to return frequently so that the doctor can also treat him actively for his neurosis.

THE NORFOLK DISTRICT MEDICAL SOCIETY

A regular meeting of the Society will be held in the Norwood Hospital, Norwood, Massachusetts, Tuesday evening, November 26, 1935, at 8:15 P.M. Tel. Norwood 1520.

Business:
Communications:

"Surgery of the Stomach." Dr. J. J. Hepburn.

"Psychotherapy in General Practice." Dr. A. A. Fenton.

"Metastasis in Cancer of the Breast." Dr. Valmore Pelletier.

Discussion.
Collation.

FRANK S. CRUICKSHANK, M.D., *Secretary.*
1236 Beacon Street, Brookline.

ARTHRITIS CLINICS AT THE ROBERT BRECK BRIGHAM HOSPITAL

A bi-monthly series of clinical meetings on the general subject of arthritis will be conducted during the winter months at the Robert B. Brigham Hospital, 125 Parker Hill Avenue, Boston. Physicians and medical students are cordially invited to attend. The next meeting will be held Wednesday, December 4, at 5:00 P.M.

The third clinic this fall was held November 13 when two patients were presented, one a fifteen year old boy with rheumatic fever and rheumatoid arthritis, the other a thirteen year old girl with Still's disease. In addition there was a demonstration of acetyl-beta-methylcholin chloride iontophoresis, a therapeutic measure which has lately attracted some attention in the treatment of chronic arthritis and peripheral vascular disease.

ROBERT T. PHILLIPS,
Resident Physician.

HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will be held in the Peter Bent Brigham Hospital Amphitheatre (Shattuck Street Entrance), Tuesday evening, November 26, at 8:15 P.M.

PROGRAM

Presentation of Cases.

The Mechanism and Effects of Abdominal Compression in the Treatment of Pulmonary Tuberculosis. By Dr. Burgess Gordon, Associate Professor of Medicine, Jefferson Medical College.

Medical students and physicians are cordially invited to attend.

MARSHALL N. FULTON, M.D., *Secretary.*

SOCIETY MEETINGS, CONGRESSES AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY, NOVEMBER 25, 1935

Monday, November 25—

*9-10 A.M. Boston Dispensary, 25 Bennet Street, Boston. Heart Clinic. Dr. S. H. Proger and Mrs. C. Janeway.

*5 P.M. Edward K. Dunham Lecture. Harvard Medical School Amphitheater, Building C.

8:15 P.M. New England Heart Association. Boston City Hospital, Amphitheater of the Mallory Institute of Pathology (Entrance at 784 Massachusetts Avenue, Boston).

Tuesday, November 26—

*9-10 A.M. Boston Dispensary, 25 Bennet Street, Boston. X-Ray Demonstration. Dr. A. Ettinger.

2:30 P.M. Pediatric Ward Visit. Massachusetts Eye and Ear Infirmary.

*8:15 P.M. Harvard Medical Society. Peter Bent Brigham Hospital Amphitheatre (Shattuck Street Entrance).

Wednesday, November 27—

*9-10 A.M. Boston Dispensary, 25 Bennet Street, Boston. Ward Cases. Dr. S. J. Thannhauser.

†12 M. Clinico-Pathological Conference. Children's Hospital.

*5 P.M. Edward K. Dunham Lecture. Harvard Medical School Amphitheater, Building C.

Friday, November 29—

*9-10 A.M. Boston Dispensary, 25 Bennet Street, Boston. Ward Cases. Dr. S. J. Thannhauser.

Saturday, November 30—

*9-10 A.M. Boston Dispensary, 25 Bennet Street, Boston. Peptic Ulcer. Dr. S. J. Thannhauser.

*10-12. Staff rounds at the Peter Bent Brigham Hospital.

*Open to the medical profession.
†Open to Fellows of the Massachusetts Medical Society.

November 21—Harvard Medical School. Lecture on "The Care of the Patient." Dr. David D. Scannell. Amphitheatre C at 5 P.M.

November 21—Medical Clinic at the Peter Bent Brigham Hospital, 3:30 P.M.

November 21—The Boston Health League and the Massachusetts Central Health Council at the Parker House, Boston, 12:30 P.M.

November 21—Clover Hill Hospital, Lawrence, Medical Meeting, 4:30 P.M.

November 22—Boston University School of Medicine Surgical Clinic at the Boston City Hospital. See page 1051.

November 22, 25, and 27—The Edward K. Dunham Lectures. Harvard Medical School. See page 1000, issue of November 14.

November 23—Clinic by Dr. S. J. Thannhauser. Boston Dispensary, 25 Bennet Street, Boston.

November 25—New England Heart Association, 8:15 P.M. Boston City Hospital, Amphitheater of the Mallory Institute of Pathology.

November 26—Harvard Medical Society. See page 1055.

December 4—Arthritis Clinics at the Robert Breck Brigham Hospital. See page 1055.

December 5-7—National Society for the Prevention of Blindness. See page 940, issue of November 7.

December 13—William Harvey Society. Beth Israel Hospital, 8 P.M.

DISTRICT MEDICAL SOCIETIES

FRANKLIN DISTRICT MEDICAL SOCIETY

Meetings are held on the second Tuesday of January, March and May at the Weldon Hotel, Greenfield, at 11 A.M.

CHARLES MOLINE, M.D., Secretary.

NORFOLK DISTRICT MEDICAL SOCIETY

November 26—See page 1055.

January 28, 1936—Hotel Kenmore at 8 P.M. Dr. Benedict F. Boland—"Cauterization of the Cervix Uteri Using Various Electrical Methods." Illustrated with lantern slides.

February 25, 1936—Massachusetts Memorial Hospitals at 8 P.M. Papers by the staff.

March 31, 1936—Hotel Kenmore, at 8 P.M. (Subject to be announced.)

May, 1936—Annual Meeting. (Place, date and subject to be announced.)

The censors meet for the examination of candidates: May 7, 1936; November 5, 1936.

FRANK S. CRUICKSHANK, M.D., Secretary.
1236 Beacon Street, Brookline, Massachusetts.

PLYMOUTH DISTRICT MEDICAL SOCIETY

January 16—Goddard Hospital. Subject and speakers to be announced later.

March 19—Plymouth County Sanatorium, South Hanson.

April 16—Brockton Hospital.

May 21—Lakeville State Sanatorium.

G. A. MOORE, M.D., Secretary.

SUFFOLK DISTRICT MEDICAL SOCIETY

December 11—Joint Meeting with the New England Heart Association at the Boston Medical Library. "Constrictive Disease of the Pericardium," Dr. Charles Sidney Burwell. Discussion: Dr. Edward D. Churchill and Dr. Paul D. White.

January 29, 1936—Joint Meeting with the Boston Medical Library at 8 Fenway. "Observations Around the World," Dr. Walter B. Cannon.

March 18, 1936—Meeting at the Boston Medical Library. "The Laboratory and Clinical Story of Fatigue," Dr. Arlie V. Bock and Dr. David B. Dill. Discussion: Dr. Donald J. MacPherson and Dr. Augustus Thorndike, Jr.

April 29, 1936—Annual Meeting at the Boston Medical Library. "The Treatment of Septicaemia," Dr. Champ Lyons. "The Pleurality of Scarlatinal Streptococcus Toxin," Dr. Sanford B. Hooker. Discussion: Dr. Hans Zinsser.

The medical profession is cordially invited to attend all of these meetings.

ROBERT L. DeNORMANDIE, M.D., President,
CHARLES C. LUND, M.D., Secretary,
FRANCIS T. HUNTER, M.D.,
Boston Medical Library.

WORCESTER DISTRICT MEDICAL SOCIETY

December 11—Wednesday evening. St. Vincent Hospital, Worcester, Mass. Dinner and scientific program. Subjects of program to be announced later.

January 8, 1936—Wednesday evening. Worcester City Hospital, Worcester, Mass. Dinner and scientific program. Subjects of program to be announced later.

February 12, 1936—Wednesday evening. Worcester State Hospital, Worcester, Mass. Dinner and scientific program. Subjects of program to be announced later.

March 11, 1936—Wednesday evening. Memorial Hospital, Worcester, Mass. Dinner and scientific program. Subjects of program to be announced later.

April 8, 1936—Wednesday evening. Hahnemann Hospital, Worcester, Mass. Dinner and scientific program. Subjects of program to be announced later.

May 13, 1936—Wednesday afternoon and evening. Annual Meeting of Society. Time, place and details of program to be announced in an April issue of the Journal.

ERWIN C. MILLER, M.D., Secretary.

BOOK REVIEWS

The Woman Asks the Doctor. Emil Novak. 189 pp. Baltimore: The Williams & Wilkins Company. $1.50.

In this book Dr. Novak has attempted to put into print his answers to the questions which the average woman patient asks her doctor about herself. He has succeeded admirably in accomplishing this purpose. Your reviewer does not know of any book which is at all comparable to it. The style is simple and readable. Every doctor will recognize the questions which have inevitably come up many times in his own practice. Dr. Novak has had the skill and the knowledge to answer them in an authoritative manner. We can recommend this book in every way, and the price brings it within the reach of any patient.

Section of Primate Physiology, Laboratory of Physiology, Yale University School of Medicine. Collected Papers, July 1, 1934-June 30, 1935. Vol. II. New Haven, Connecticut.

This second volume of collected reprints from the very active physiological laboratory of the Yale Medical School is a fitting tribute to the work of Professor John F. Fulton, the head of the department. The work of this laboratory indicates that under his direction productive research is being carried forward along many lines of neurophysiology. Thirty new papers published in the course of a year are conveniently bound for easy reference, with an adequate table of contents.